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REGULATION OF FUNCTIONAL FOODS IN UKRAINE AND THE WORLD. PROSPECTS FOR THE USE OF POSTBIOTICS AS FUNCTIONAL INGREDIENTS

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Abstract. Functional food allows to individualize the characteristics and necessities of each person. Over the past few decades, the demand for products that have a positive impact on human health has exploded worldwide. The market for functional foods in developed countries is estimated at USD 300 billion, which makes this sector attractive for investment. Accordingly, the production of functional foods and ingredients needs to be regulated at the state level. There is no harmonization in the definitions of functional foods and their classification at both the global and state levels. Despite the fact that the concept and terminology of functional food and the means of achieving it is well-established, the term "functional food" is often absent in the legislative acts of countries that actively produce functional foods, and the term "health-related food" is used instead. As a rule, health-related foods are subject to quality and safety requirements that are identical to those of conventional food products. Exceptions are regulations that establish rules for labeling FFPs and statements regarding their physiological effects or the content of a particular ingredient that may affect physiological aspects. In Europe and the USA, much attention is paid to the safety of "health-related food" and the novel food products. European Food Safety Authority and the US Food and Drug Administration require sponsors to submit information on the composition of multiple batches of a product to support safety evaluations for novel foods and Generally Recognized as Safe (GRAS) ingredients. In Ukraine, the legal status of the terms "functional food product" and dietary supplement was regulated by Law of Ukraine 771 "On Basic Principles and Requirements for Food Safety and Quality", but in the version of this law dated 16.01.2020, this term was excluded, the term "dietary supplement" was edited and the term "novel food product or ingredient" was included, which is related to the process of harmonization of Ukrainian and European legislation in the food sector. In 2020, the Ministry of Health of Ukraine approved Order No. 1145 "On Approval of the Requirements for Nutrition Claims and Health Claims for Food Products", which regulates the following concepts: claims and conditions for their use; health claims allowed to be used in food labeling and advertising, except for claims about reducing the risk of diseases and claims related to the development and health of children; claims about reducing the risk of diseases and claims related to the development and health of children. Unfortunately, Ukrainian regulations do not contain claims and conditions for the use of claims about pro- and prebiotics that have GRAS status worldwide. Particular attention should be paid to the possibility of using postbiotics as functional food ingredients with immunological activity.

Keywords: functional foods, ingredients, regulation, claims, postbiotics, safety.

Introduction. Formulation of the problem

The concept of the dependence of a person's health on their nutritional status is evolutionarily established. Given the latest trends in the development of nutrition and the theory of optimal nutrition, the development of specialized and functional products is gaining significant development [1-4]. The directions of creating technologies for this category of food products are multivector and depend on specific tasks aimed to overcome various pathologies through nutritional support [1,2,4,6-9].

Functional nutrition allows to individualize the features and needs of each person, to prevent the lack of essential food components that can occur due to certain dietary restrictions associated with diseases of various etiologies, allergic disorders, and an intense lifestyle that does not allow for regular and adequate nutrition [1,2,4].

Over the past few decades, the demand for products that have a positive impact on human health has exploded worldwide. This growth has been caused by socio-economic and scientific factors, including an increase in population and disposable income. The healthy food market is growing rapidly due to advances in dietary bioactive ingredient technology and the study of their impact on various aspects of human health at the systemic and molecular levels. The market for functional food products (FFPs) in developed countries is estimated at about $300 billion (Fig. 1).

According to Functional Foods Global Market, in the United States, which is the leader among FFPs producers, the market for this type of product will grow by more than 30% by 2025 compared to 2021. One of the main reasons for this is the global pandemic, the decline in the immune status of the population, etc. This trend leads to high investment attractiveness in this area [10,11].

In Ukraine, according to rather approximate data (since no such statistics are kept), the share of functional foods does not yet exceed 3–5% of all known food products. However, the demand for functional foods and ingredients in Ukraine can be predicted by drawing a parallel with the dietary supplements market. According to the analysis of pharmacy sales of dietary supplements (DS), this class of products demonstrates fairly stable dynamics. In 2019, sales of DS in Ukraine amounted to about UAH 4.2 billion, and in 2020 – already UAH 8 billion [12].

A significant share of the DS market in Ukraine and the world is occupied by immunologic supplements of plant and/or microbial origin [12]. The growth in demand for such products is due to the decline in the immune status of the population, including due to a number of events that occurred during 2020–2023. Among immunological agents, products of postbiotic origin deserve special attention [13-16]. The study of the immunological properties of postbiotics has been gaining momentum in recent years, the mechanisms of immunological action of most of them have already been substantiated, their effectiveness in vitro and in vivo has been proven, and a number of pharmacological preparations based on them have been developed [16-24]. At the same time, research is ongoing on the possibility of including products of postbiotic origin in the composition of DS and functional food ingredients [25-29]. There are also no regulatory references to claims about their nutritional value and health benefits.

Ukraine, as a developing country in Eastern Europe and a country that is rich in the necessary resources for the production of larger volumes of functional products, is promising for investing in new projects for the production of FHP, and for the development of existing ones. Of course, the production and circulation of FFPs and ingredients need to be regulated at the state level. First of all, we are talking about requirements for the quality and safety of FFPs, as well as the structuring of information (claims) on the packaging. Manufacturers should be guided by the requirements and regulations for FFPs approved at the state level. In addition, the modern consumer is quite conscious, interested in the composition of the product, the presence or absence of certain food ingredients, physiologically active components, etc. For the sake of correct labeling and informing consumers, in the developed countries-leaders in the production of FFPs, special guidelines and regulations for the application of various statements about the composition, structure and impact on health have been developed. In Ukraine, there is currently uncertainty with the placement of certain FFPs claims on packaging, as there is no systematization of such concepts at the governmental level, and according to the Law of Ukraine 2639 "On Information for Consumers on Food Products" Article 4, paragraph 4 – "information on food products should not attribute to any food products, except for natural mineral waters and food products for special medical purposes, properties that contribute to the prevention or treatment of diseases, or refer to such properties".

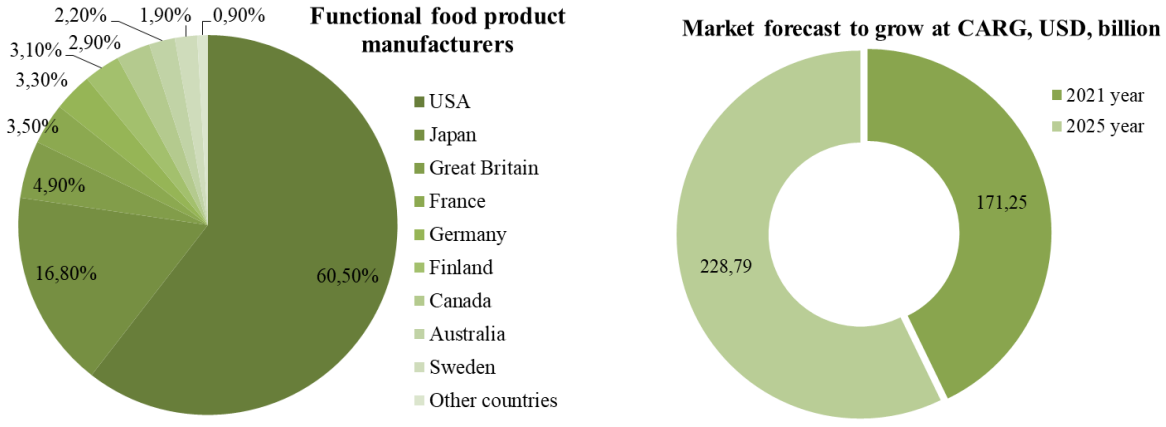

Fig.1. Global Functional Food Market [10,11]

Therefore, **the purpose** of this paper is to analyze the existing regulation practices of the production and labeling of FFPs in the international space and the state of this issue in Ukraine, as well as to study the possibility of classifying postbiotics as functional food ingredients.

Research tasks:

- analysis of the evolution of statements about functional nutrition;
- study of the peculiarities of regulation of FFPs by the leading countries of their production (USA, Japan, European countries);
- study of the current state regulation of the circulation of FFPs and DSs in Ukraine and future prospects;
- analysis of studies devoted to the possibility of using postbiotics as functional food ingredients.

The evolution of functional food claims

Technological progress provoked the transformation of eating habits and preferences, which in turn became the impetus for the development of food science, improvement of technologies and nutritional composition of food. If even before the middle of the 20th century, food was positioned as a substance for maintaining the main physiological functions of the body, then starting from the 2nd half of the 20th century, consumers preferred food that did not require long cooking, which significantly saves time. This was preceded by a significant expansion of the assortment and mass production of food products, but along with this, the concept of biological value was somewhat leveled [30-31].

With the development of nutrition science, knowledge of the chemical composition of foods, the metabolism of nutrients, their physiological activity, and the possibility of correcting deficiency and pathological conditions with food has been improving. Therefore, at the end of the twentieth century, strategic programs for the introduction of functional food and the development of functional food products were created in many countries of the world [7,9,32-33].

Such projects have been operating in Japan since 1984, thanks to which the popular concept of FOSHU (Foods for Specified Health Use) was developed. In Europe, as early as 1986, the development of the program "Scientific bases of functional food in Europe" was started, which became a prototype for similar developments in the future. Most economically developed countries (Japan, USA, Holland, Great Britain, China, Canada, and others) have developed programs that regulate the design and using of functional products. To address these problems, Ukraine has implemented the national programs "Healthy Nation", "Health-2020: Ukrainian Dimension", "Biofortification and Functional Products Based on Plant-Based Raw Materials for 2012-2016" [9,34-35].

In terms of functional food, the following terms are most widely used: functional food product (FFP), functional food ingredient (FFI), ietary supplement (DS). There is no harmonization in the scientific definitions and classifications of these concepts at both the global and national levels.

The EU food law defines functional foods as "any modified food or food ingredient that may have a beneficial effect on human health, in addition to the effects of the traditional food substances it contains" [39].

The European Food Safety Authority (EFSA) defines functional foods as "A food, which beneficially affects one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease. A functional food can be a natural food or a food to which a component has been added or removed by technological or biotechnological means, and it must demonstrate their effects in amounts that can normally be expected to be consumed in the diet" [40].

The Functional Food Center (FFC) proposes a definition for FFs as "Natural or processed foods that contain biologically-active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms" [1].

Canada Government proposes next definition for FFs "A functional food is similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional function" [41].

According to Korean legislation "health/functional food" refers to food supplements containing nutrients or other substances (in a concentrated form) that have a nutritional or physiological effect whose purpose is to supplement the normal diet [42].

In a paper [43] FFs is defined as "A food that beneficially affects one or more target functions in the body beyond adequate nutritional effects in a way that is relevant to either an improved state of health and well-being and/or reduction of risk of disease: Not a pill, a capsule, or any form of dietary supplement consumed as part of a normal food pattern".

Gul and other define FFs as "Functional foods are the foods or dietary components consumption of which may have associated health benefits beyond the basic nutritional properties that the foods possess" [44].

The definition of the concept of FFP was provided by many scientists of the post-Soviet space [2,4,6,7,9]. The existing definitions do not have a fundamental difference and correlate with each other. Summarizing them, it is possible to give the following

definition of the concept "FFPs are products that provide human needs for energy, plastic materials, nutrients, compensate for the deficiency of essential substances, support the normal functional activity of the body, reduce the risk of various diseases and can be consumed regularly, contain ingredients, which increase resistance to various diseases, allow you to maintain an active lifestyle for a long time, prevent diseases and slow down the aging of the body, adapt to anthropogenic and social conditions, the effectiveness of which has been proven by the results of medical and biological research".

The production of functional food products requires the understanding and systematization of categories, which includes this concept. One of the main tasks in the way of FFPs regulation is to ensure the transparency of their biological action and safety.

Study of the peculiarities of FFs regulation by the countries leading their production (USA, European countries)

Despite the fact that the concept and terminology of functional food and the means of achieving it is well-established, the term "functional food" is often absent in the legislative acts of countries that actively produce functional foods, and the term "health-related food" is used instead. As a rule, health-related foods are subject to quality and safety requirements that are identical to those of conventional food products. Exceptions are regulations that establish rules for labeling FFPs and statements regarding their physiological effects or the content of a particular ingredient that may affect physiological aspects.

American regulation

The main control over the quality and safety of food products, biologically active additives, including "health-related food" in the United States is vested in the FDA (Food and Drug Administration).

The required information that must appear in the food and food supplements' package (e.g. data about the manufacturer and the distributor) as well as the nutrition labeling including health-related claims are under the Nutrition Labeling and Education Act (last amendment in 2016), codified in the Title 21 of the Code of Federal Regulations (21 CFR) (1967). Regarding health-related claims, there are three approved categories: "nutrient content claims", "structure/function claims" and "health claims" (United States Congress, 1990) [45].

Nutrient content claims are those that express or imply the level of a nutrient in a food product (food and food supplements). Expressed claims directly inform about the level or range of the nutrient, for instance "low sodium" and "contains 100 calories". Implied claims can be those that suggest the absence of the nutrient or its presence in a certain amount using terms like "free", "reduced/less" and "high".

Structure/function claims are those that express the effect of a nutrient/ingredient on the structure or function of the organism without making a reference to a disease. These claims have historically appeared in the labeling of food, food supplements and even medicines.

Health claims are those that express a relation between a food component or a food supplement ingredient and a disease or healthrelated condition. The diseases mentioned in the claim must be those for which the American population or a specific population group (e.g. elderly people) is at risk, without including those caused by nutrient deficiencies (vitamin C – scurvy; vitamin D – rickets; vitamin B2 – pellagra; iron – anemia).

Authorized health claims can suggest or imply that a food or food component may reduce the risk of a disease or a health-related condition. Any food company interested in marketing its products with a new health claim describing or suggesting new health effects must make a request to the FDA as a pre-marketing approval is mandatory. Authorized health claims are only approved under an extensive review of the current scientific literature. Randomized and controlled clinical intervention trials are considered as the most reliable proofs (also called "the gold standard") to confirm the relationship between the specific component included in the food product, and the health.

Ehe FDA has approved 18 health claims. Significant Scientific Agreement (SSA) health claims can be made on food and food supplements whereas FDMA health claims can only appeared on food [45,46]. Table 1 shows examples of some wording SSA health claims and FDMA health claims.

Professor Martirosyan and Functional Food Center (Dallas, TX, USA)have been proposed a multi-step process for the development of functional food products and ways by which to bring them to market without means to classify established items. The newest steps focus on themes of transparency by the publishing of peer-reviewed articles for the functional food product as mandatory for accreditation. In doing so, this will provide greater access to information for the functional food market, as well as, acceptance and trustworthiness of functional claims. Additionally, the Functional Food Center has created a new system for categorizing functional foods. The new categorization system uses improved research on epidemiological and after market studies, and evaluates the quality of evidence for the functional food product as A, B, or C. A classification of A denotes the completion of aftermarket research, epidemiological studies, and certification of functional food status. Classification B denotes completion of epidemiological studies and certification of functional food status. Lastly, C indicates that the product has only been certified as functional [47].

Table 1 – Examples wording SSA health claims and FDMA health claims

Component/ingredient – disease/health-related condition Model claim statement(s)	Component/ingredient – disease/health-related condition Model claim statement(s)
FDMA health claims	
Whole Grain Food and Risk of Heart Disease and Certain Cancers	Diets rich in whole grain food and other plant food and low in total fat, saturated fat, and cholesterol may reduce the risk of heart disease and some cancers
Whole Grain Food with Moderate Fat Content and Risk of Heart Disease	Diets rich in whole grain food and other plant food, and low in total fat, saturated fat, and cholesterol may help reduce the risk of heart disease".
Potassium and the Risk of High Blood Pressure and Stroke	Diets containing food that are a good source of potassium and that are low in sodium may reduce the risk of high blood pressure and stroke
Saturated Fat, Cholesterol, and Trans Fat, and Reduced Risk of Heart Disease	Diets low in saturated fat and cholesterol, and as low as possible in trans fat, may reduce the risk of heart disease
Substitution of Saturated Fat in the Diet with Unsaturated Fatty Acids and Reduced Risk of Heart Disease	Replacing saturated fat with similar amounts of unsaturated fats may reduce the risk of heart disease. To achieve this benefit, total daily calories should not increase
SSA health claims	
Calcium and osteoporosis and calcium, vitamin D, and osteoporosis	"Adequate calcium throughout life, as part of a well-balanced diet, may reduce the risk of osteoporosis" and "Adequate calcium and vitamin D, as part of a well-balanced diet, along with physical activity, may reduce the risk of osteoporosis".
Dietary fat and cancer	"Development of cancer depends on many factors. A diet low in total fat may reduce the risk of some cancers".
Sodium and hypertension	"Diets low in sodium may reduce the risk of high blood pressure, a disease associated with many factors".
Dietary saturated fat and cholesterol and risk of coronary heart disease	"While many factors affect heart disease, diets low in saturated fat and cholesterol may reduce the risk of this disease"
Fiber-containing grain products, fruits, and vegetables and cancer	"Low fat diets rich in fiber-containing grain products, fruits, and vegetables may reduce the risk of some types of cancer, a disease associated with many factors".

European regulation

There is also no officially defined term functional food in the European Union, but in 2006, Sweden developed the Code of Practice for the Labeling of Foods with Health Claims, which clearly regulates claims about the functions of certain nutrients and the requirements for their use. After that, the EU Regulation 1924/2006 became the first food-related legislation in the EU and applies to "food" and "food (dietary) supplements". Thus, FFPs and foods with any health information related to vitamins, minerals and/or other substances in labeling, presentation and/or advertising must comply with the special requirements set out in Regulation (EC) 1924/2006 [45,48].

The article 2.2 of Regulation (EC) 1924/2006 establishes three categories of claims: "nutrition claims", "health claims" and "reduction of disease risk claims". All claims refer to the product as a food and/or food supplement. In any case they will suggest or imply that the product in question has preventive, therapeutic or curative properties of a human disease.

Nutrition claims are those that state, suggest or imply that a food has specific beneficial nutritional properties due to its caloric value, the nutrients or other substances, that it contains in a reduced or increased proportion, or directly that it does not have. For instance, "high in vitamins, fibre or proteins" or "low in calories, salt or sugar".

Health claims are considered those that affirm, suggest or imply that there is a relation between a food category, a food or one of its components, and health. As health claims could have a significant impact on the consumers dietary behaviour, important matters should be considered. Any claim which describes or suggests a new health-related benefit for the human organism is required to go through a pre-marketing approval [45,49]

Reduction of disease risk claims are health claims that state, suggest or imply that the consumption of a food category, a food or one of its components, can significantly reduce a risk factor in the development of a human illness. Given that diet is an important risk factor in the development of chronic diseases, specific labeling requirements should be applied [45].

European food legislation is also represented by the following regulations:

– Regulation (EC) No. 178/2002 of the European Parliament and of the Council of 28 January 2002 laying down the general principles and

requirements of food law, establishing the European Food Safety Authority and laying down procedures in matters of food safety [50].

– Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements [51].

– Regulation (EC) No. 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods [52].

– Regulation (EU) No. 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No. 41/2009 and (EC) No 953/2009 [53].

– Regulation (EU) 2015/2283 of the European Parliament and the council of 25 November 2015 on novel foods, amending Regulation (EU) No. 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No. 1852/2001 [54].

Fig. 2 summarizes the structure of claims regulation on health-related food in USA and Europe.

Great importance is attached to the safety of health-related food in both the US and Europe. European Food Safety Authority (EFSA) and the US Food and Drug Administration (FDA) require sponsors to submit information on the composition of multiple batches of a product to support safety evaluations for novel foods and Generally Recognized as Safe (GRAS) ingredients (respectively). Production of consistent products begins with the harvesting or gathering of the material that will become a functional ingredient [45-46].

Regulation of functional foods and dietary supplements in Ukraine

Today, the production of DS, FFI and FFP, etc. is subject to the Law of Ukraine 771 "On Basic Principles and Requirements for Food Safety and Quality", which sets out the requirements for prerequisite programs that implement good manufacturing and hygiene practices, as well as the main steps and principles for implementing the HACCP (Hazard analysis and critical control point) system. The State Service of Ukraine on Food Safety and Consumer Protection and its territorial bodies are responsible for supervising the production and circulation of DS.

The production of dietary supplements is also regulated by the Order of the Ministry of Health of Ukraine No. 1114 "On Approval of Hygienic Requirements for Dietary Supplements" dated 19.12.2013, which sets out requirements for dietary supplements, their labeling, and lists vitamins and minerals and their forms allowed for use in the production of dietary supplements. Unfortunately, this list does not include such generally recognized nutraceuticals as dietary fiber, PUFAs, essential amino acids and other compounds with high physiological activity and beneficial effects on the human body.

Another regulatory act that should be relied upon in the production of DS and FFI is Order of the Ministry of Health of Ukraine No. 1073 of 03.10.2017 "Norms of physiological needs of the population of Ukraine in basic food substances and energy". There is also Order of the Ministry of Health of Ukraine No. 368 of 13.05.2013 "State Hygienic Rules and Regulations "Regulation of Maximum Levels of Certain Contaminants in Food Products".

In order to harmonize the food legislation of Ukraine and the EU, since 2014, legislative acts have been transformed, new terms and definitions of the main concepts related to functional food have been introduced and improved. The evolution of terms related to "health related food" is presented in Table 2.

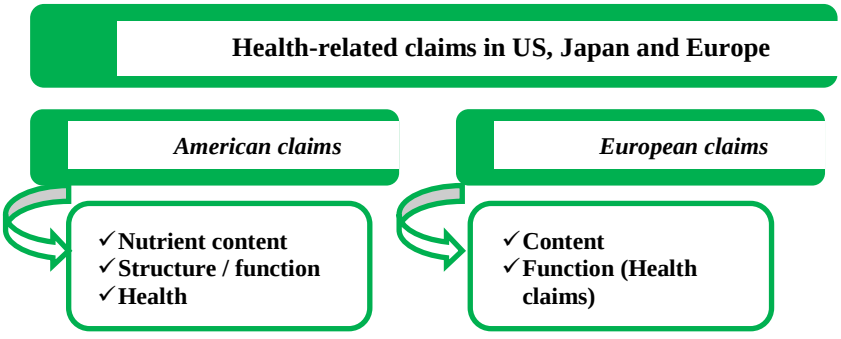

Fig. 2. the structure of claims regulation on health-related food in USA and Europe

Table 2 – Terms and definitions of concepts related to functional food of the Law of Ukraine 771 "On Basic Principles and Requirements for Food Safety and Quality"

Edition of 06.09.2005	Edition of 31.03.2023
Functional food product is a food product that contains medicines as a component and/or is offered for the prevention or mitigation of a human disease	Definition is missing
Dietary supplement is a vitamin, vitamin-mineral or herbal supplements separately and/or in combination in the form of pills, tablets, powders, taken orally with food or added to food within the limits of physiological norms, for additional use of these compared to normal nutrition substances; dietary supplements also contain or include various substances or mixtures of substances, including protein, carbohydrates, amino acids, edible oils and extracts of plant and animal materials, which are considered necessary or useful for human nutrition and general health	**A dietary supplement** is a food product consumed in small defined quantities in addition to the usual food diet, which is a concentrated source of nutrients, including proteins, fats, carbohydrates, vitamins, minerals (this list is not exclusive), and is made in the form tablets, capsules, dragees, powders, liquids or other forms
Food products for special dietary consumption (use) - food products that are specially processed or designed to meet specific dietary needs that exist due to a specific physical or physiological condition of a person and/or a specific disease or disorder, and which are sold as such, including baby food, food for athletes and the elderly	**Food product for special medical purposes** is a food product specially designed and manufactured for feeding patients (including infants and young children), which should be consumed as prescribed by a doctor in a healthcare facility and/or outside it
Definition is missing	**A weight control food product** is a specially designed and manufactured food product intended for consumption while following a low-calorie diet for weight loss, which, when consumed in accordance with the instructions of the market operator, replaces the daily diet
Definition is missing	**Novel food product or ingredient** means a food product or ingredient that differs significantly from conventional food products or ingredients available on the market and must be evaluated in terms of its impact on consumer health

Thus, the current version of the Law of Ukraine No. 771 does not define "functional food product" and "functional food ingredient", but instead uses the terms "dietary supplement" and "novel food product or ingredient", which to some extent allow the legitimate use of functional food principles in Ukraine.

The current version of the law introduces a new term "novel food product", but its interpretation in the glossary is not sufficient to fully understand its meaning. In 2021, a draft Law of Ukraine "On Amendments to Certain Laws of Ukraine on Food Products and Other Objects of Sanitary Measures" was introduced, including the Law of Ukraine "On Basic Principles and Requirements for Food Safety and Quality". This draft law provides quite a good explanation for the introduction of the term "novel food product". The implementation of this draft law will ensure that the regulatory framework in the field of food legislation of Ukraine is brought in line with the requirements of Regulation EU No. 1924/2006 of the European Parliament and of the Council.

In 2020, the Ministry of Health of Ukraine approved Order No. 1145 "On Approval of the Requirements for Nutrition Claims and Health Claims for Food Products", which greatly facilitated the work of functional food producers.

This regulatory document contains the following lists:

– list of nutritional claims and conditions for their use (30 items);

– list of health claims allowed to be used in food labeling and advertising, except for claims about reducing the risk of diseases and claims related to the development and health of children (239 items);

– list of claims about reducing the risk of diseases and claims related to the development and health of children (25 items) (examples are given in Tables 3-5).

Thus, after analyzing the current state of regulation of functional foods in Ukraine, we can note significant progress compared to the standards of a decade ago. First of all, this progress is due to the harmonization of Ukrainian legislation with European legislation, which is a prerequisite for joining the European Union. Thus, the statements and definitions of Ukrainian regulations on "health related food" today are fully correlated with the European ones, namely, the need to cover information on Content and Function (Health claims) of functional foods. Unfortunately, Ukrainian regulations do not contain claims and conditions for the use of claims about pro- and prebiotics that have GRAS status worldwide. Particular attention should be paid to the possibility of using postbiotics as functional food ingredients with immunological activity.

Table 3 – List of nutrition claims and conditions for their application*

Nutritional claims	Conditions for the use of nutrition claims
Low-calorie product / Product with low energy value	The claim that a food product is low-calorie (with low energy value) and another claim likely to have the same meaning for the consumer may only be made if the food product does not contain more than 20 kcal (80 kJ) per 100 ml for liquid foodstuffs or more than 40 kcal (170 kJ) per 100 g for other foodstuffs. For table sweeteners, the upper limit is 4 kcal (17 kJ) per serving, or the equivalent of no more than 6 g of sucrose (approximately one teaspoon of sucrose)
Product with reduced calorie content / Product with reduced energy value	The claim that the food product has a reduced caloric value (energy value) and another claim likely to have the same meaning for the consumer may be made only if the caloric value (energy value) is reduced by at least 30 percent, indicating the characteristics that lead to to a decrease in total caloric content (energy value)
With low sugar content	A claim that the food is low in sugar and another claim likely to have the same meaning for the consumer may only be made if the food contains no more than 2.5 g of sugar per 100 ml for liquid foods products or 5 g of sugar per 100 g for other food products
Does not contain sugar	The claim that the food is sugar-free and another claim likely to have the same meaning for the consumer may only be made if the food contains no more than 0.5 g of sugar per 100 g or 100 ml
With a high protein content	A claim that a food is high in protein and another claim likely to have the same meaning for the consumer may only be made if at least 20 percent of the energy value (calories) of the food is provided by protein
A source of omega-3 fatty acids	The claim that the food is a source of omega-3 fatty acids and another claim likely to have the same meaning for the consumer may only be made if the product contains at least 0.3 g of alpha-linolenic acid per 100 g and per 100 kcal, or at least 40 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal
High content of omega-3 fatty acids	A claim that a food product is high in omega-3 fatty acids and another claim likely to have the same meaning for the consumer may only be made if the product contains at least 0.6 g of alpha-linolenic acid per 100 g and per 100 kcal, or at least 80 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal.
High content of polyunsaturated fats	A claim that a food is high in polyunsaturated fat, and another claim likely to have the same meaning to the consumer, may be made only if the food contains at least 45 percent of fatty acids derived from polyunsaturated fat, provided that that polyunsaturated fats provide more than 20 percent of the energy value (calorie) of a food product.

Table 4 – List of claims about health benefits allowed for use in labeling and advertising of food products, except for claims about reducing the risk of diseases and claims related to the development and health of children*

Nutrient, substance, food	Claim	Terms of claim use
Activated carbon	Activated charcoal helps to reduce excessive flatulence after eating	The claim may be used only for a food product containing 1 g of activated carbon per defined serving. To use this claim, the consumer must be informed that a positive effect can be obtained by consuming 1 g at least 30 minutes before and 1 g immediately after a meal.
Arabinoxylan derived from wheat endosperm	Eating arabinoxylan with food helps to reduce the rise in blood glucose levels after meals	The claim may be used only for a food product containing at least 8 g of arabinoxylan (AX), a fortified fiber derived from wheat endosperm (at least 60 percent AX by weight) per 100 g of available carbohydrates per defined serving. To use this claim, the consumer must be informed that a positive effect can be obtained by consuming arabinoxylan (AX), a fortified fiber derived from wheat endosperm, directly with food
Dietary fiber (fiber) of barley	Dietary fiber (fiber) of barley helps to increase feces	The claim may only be used for a food product that has a dietary fiber (fiber) content as high as specified in the conditions for the application of the nutrition claim "HIGH IN DIETARY FIBER (FIBER)".
Beta glucans	eta-glucans help maintain normal blood cholesterol levels	The claim may be used exclusively for a food product containing at least 1 g of beta-glucans derived from oats, oat bran, barley, barley bran or a mixture of these beta-glucan sources in a given portion. To use this claim, the consumer must be informed that a positive effect can be obtained by daily consumption of 3 g of beta-glucans derived from oats, oat bran, barley, barley bran or a mixture of these beta-glucans.
Chitosan	Chitosan helps to maintain normal blood cholesterol levels	he claim can be used for a food product whose consumption provides a daily intake of 3 g of chitosan. To use this claim, the consumer must be provided with information that a positive effect can be obtained by daily consumption of 3 g of chitosan.

*full list and its description see in Order No. 1145of the Ministry of Health of Ukraine "On Approval of the Requirements for Nutrition Claims and Health Claims for Food Products"

Table 5 – List of claims about reducing the risk of diseases and claims related to children's development and health*

Nutrient	Claim	Terms of claim use
Alpha-linolenic acid (ALA) and linoleic acid (LA), essential fatty acids	Essential fatty acids are essential for the normal growth and development of children	The consumer should be informed that the beneficial effect is achieved with a daily intake of 2 g of alpha-linolenic acid and a daily intake of 10 g of linoleic acid
Barley beta-glucans	Barley beta-glucans have been proven to lower/reduce blood cholesterol levels.	The consumer must be informed that the beneficial effect is achieved with a daily intake of 3 g of barley beta-glucan.
	High cholesterol is a risk factor for coronary heart disease	The claim may be used for food products containing at least 1 g of barley beta-glucan per quantified serving
Protein	Protein is essential for normal growth and development of bones in children	The statement can only be used for food products that are at least a source of protein, as specified in the conditions for the use of the statement "PROTEIN SOURCE" in Annex 1 to these Requirements
Vitamin D	Vitamin D helps reduce the risk of falls associated with postural instability and muscle weakness. Falls are a risk factor for bone fractures among men and women 60 years and older	The claim can only be applied to dietary supplements that provide at least 15 mcg of vitamin D per day. The consumer is informed that the beneficial effect is achieved with a daily intake of 20 mcg of vitamin D from all sources. This statement is applicable to vitamin D supplements only for those intended for men and women 60 years of age and older
Folic acid	Folic acid supplementation increases maternal folate status. Low maternal folate status is a risk factor for neural tube defects in the developing fetus	The claim can only be applied to dietary supplements that provide at least 400 mcg of folic acid per day. Consumers should be informed that the target population is women of childbearing age and that the beneficial effect is achieved with a daily dose of 400 mcg of folic acid for at least one month before and up to three months after conception

*full list and its description see in Order No. 1145of the Ministry of Health of Ukraine "On Approval of the Requirements for Nutrition Claims and Health Claims for Food Products"

Postbiotics as functional food ingredients

Postbiotics is a new definition and classification of "biotic" drugs [27-30].

Some disadvantages of probiotic drugs, namely, the possibility of side effects such as instability in the gastrointestinal tract, spread of antibiotic resistance genes, virulence, risk of sepsis in premature infants, opportunistic properties, and obstruction of normal colonization of the commensal microflora [55-56], provoked the search for alternative substances that would have the positive biological effects of probiotic cultures but at the same time be devoid of the above negative phenomena.

Since most of the biological effects of probiotics are provided by their metabolic products, structural components of outer membranes and cell walls, since 1986 there have been some suggestions about the feasibility of using these objects as functional and physiological components and studying their properties [28,29].

The products of metabolism and processing of probiotic cultures did not have an unambiguous name and definition at the first stages of research. In the literature, there were terms such as "paraprobiotics", "non-viable microbial cells", "fermented infant formula", "metabiotics", which to some extent met the definition of postbiotics.

The term "postbiotic" first appeared in 2012, Katerina Tsilingiri and her co-authors define postbiotics as "probiotics and their metabolic products" that are proposed to be used as food supplements for healthy gut homeostasis, as well as therapeutic agents for inflammatory bowel disease [57].

In 2013, Shenderov defined "metabiotics" as "structural components of probiotic microorganisms and/or their metabolites and/or signaling molecules with a specific chemical structure that can optimize host-specific physiological functions, regulators of metabolic and/or behavioral reactions associated with the activity of the host's commensal microbiota" [58].

J. Aguilar-Toala (2018), Carrie A. M. Wegh (2019), Przemysław Tomasik (2020) in their works unanimously use the term "postbiotics" and give common features of the definition and possible components of postbiotics, namely: "postbiotics may contain bacterial lysates, cell surface proteins, bacterial enzymes and peptides, metabolites, short-chain fatty acids, teichoic acids, peptidoglycan neuropeptides, muropeptides derived from peptidoglycan, exopolysaccharides, and lower organic acids" [26-29].

The advantages of postbiotics in terms of safety, biological and pharmaceutical properties compared to probiotics include no risk of translocation from the intestinal lumen to the bloodstream, appropriate absorption, metabolism, signal transduction to various organs and tissues in the host and the implementation of several biological reactions, higher stability, and the possibility of standardization. Postbiotics maintain the host's endogenous commensal microflora, which positively affects the gut microbial ecosystem, in contrast to the introduction of exogenous probiotic

strains, which can be considered a safe alternative for regulating the gut microbiome and for use in the functional food and pharmaceutical industries [59-64].

Thus, postbiotics are free from the risks associated with the administration of live probiotic bacteria, have the advantage of a clear chemical structure, defined safe dose parameters, and a longer shelf life, which can affect the physiological functions of the macroorganism [65-66].

Postbiotic substances contain various metabolites and signaling molecules that exhibit a wide antibacterial spectrum and immunomodulatory effects [65-66], which leads to the study of the possibility of their inclusion in FFP and DD as a functional and physiological ingredient of immunological action. These products can be recommended for use by the population with a reduced immune status.

The study of the biological properties of postbiotics has become widespread.

Work [61] reported that the use of short-chain fatty acids from *Bifidobacterium breve* CNCM I-4035 contributed to the reduction of proinflammatory cytokines through TLR activation in human dendritic cells infected with *Salmonella typhi*.

Residues of probiotic cellular structures are also important tools for regulating immune function. Study [62] demonstrated that D-alanilization of teichoic acid from *Lactobacillus plantarum* WCFS1 has a positive effect on the generation of regulatory T cells in healthy mice.

The authors of the work [63], considering the effect of bacteria of the genus *Lactobacillus* on the immune functions of the body, noted that stimulation of cytokine production is possible not only in the presence of living microorganisms, but also inactivated ones.

In experiments performed on laboratory animals, it was shown that inactivated lactic acid bacteria, such as *L. delbrueckli, L. acidophilus, L. casei*, can stimulate immune responses, including phagocytosis, natural killer activity, and the production of antibody-forming cells in mice [64].

Along with enhancing anti-infective immunity, postbiotics also stimulate antitumor immunity. The antitumor effect was first demonstrated by I.G. Bogdanov et al. The authors found that the administration of culture filtrates of *L. Delbrueckii subsp. Bulgaricus* (LB 51) to mice with Crocker's sarcoma led to complete disappearance of the tumor in 59.3% of animals. Similar results were obtained with Ehrlich's carcinoma after 4 injections of L. *bulgaricus* culture filtrate: tumor disappearance was observed in 45.6% of experimental animals [67].

There are a number of pharmacological products with proven physiological activity based on postbiotics, namely, bacterial lysates of probiotic cultures, minimal fragments of peptidoglycans (muropeptides) and their synthetic analogues.

"Imudon" (Solvay Pharma, France) is a multicomponent preparation that contains lysates of 13 species of bacteria, among which the genus Lactobacillus is represented by 4 species [21]. "Imudon" is available in the form of resorbable tablets for topical use in dentistry. It activates phagocytosis, promotes the effective formation of antibodies, optimizes the functioning of the immune system, stimulates the antigenic properties of salivary lysozyme, increases the number of immunocompetent cells, and increases the secretion of salivary IgA.

"Brohomunal" (Slovenia) is a capsulated form of lysates of 8 types of bacteria, stimulates peritoneal macrophages, increases the number of T lymphocytes and antibodies IgA, G, M. Indications for the use of this drug are infectious and inflammatory diseases of the respiratory tract [22].

"Hylak Forte" (MERCKLE, Germany) contains metabolic products of *Lactobacillus acidophilus, Lactobacillus helveticus, Escherichia coli, Enterococcus faecalis*. "Hilak Forte" regulates the balance of intestinal microflora and normalizes its composition. Due to the content of metabolic products of normal microflora in the drug, it helps to restore normal intestinal microflora biologically and allows to preserve the physiological and biological functions of the intestinal mucosa [23].

Liasten (Enzyme, Ukraine) is an active substance glucosaminylmuramyl pentapeptide (N-acetylglucosaminyl-N-acetylmuramyl-L-alanyl-D-glutamyl-L-lysyl-D-alanyl-L-aspartate), belongs to immunomodulators of natural origin with a wide spectrum of action. It is a fragment of the lactobacillus cell wall, stimulates macrophage function and normalizes the number of T-lymphocytes, activates monocyte-macrophage cells, phagocytosis, increases the activity of lysosomal enzymes, production of reactive oxygen species, and enhances the cytotoxic effect of macrophages against cells infected with viruses, bacteria, and tumor cells [24].

Thus, the use of postbiotic drugs has become widespread in the pharmaceutical industry, and as a rule, a local immunotropic effect is provided when using intranasal or tablet forms. The systemic immunotropic effect occurs when injectable drugs of postbiotic origin are used.

Recently, there have been scientific assumptions about the possibility of using postbiotics in functional food [26-39], and the question arises as to its feasibility in terms of the expression of the systemic physiological effect of postbiotics when consumed orally.

Previously, it was reported that postbiotics exhibit their biological activity limited to the gastrointestinal tract [57,68]. Then it was noted that some of them can overcome the intestinal barrier and exhibit systemic antihypertensive, hypocholesterolemic and antioxidant activity [26,27]. But later, a number of studies have shown that bacterial low molecular weight cellular structures, namely muropeptides, are able to cross the intestinal barrier and exhibit systemic immunological effect (Fig. 3) [69-70].

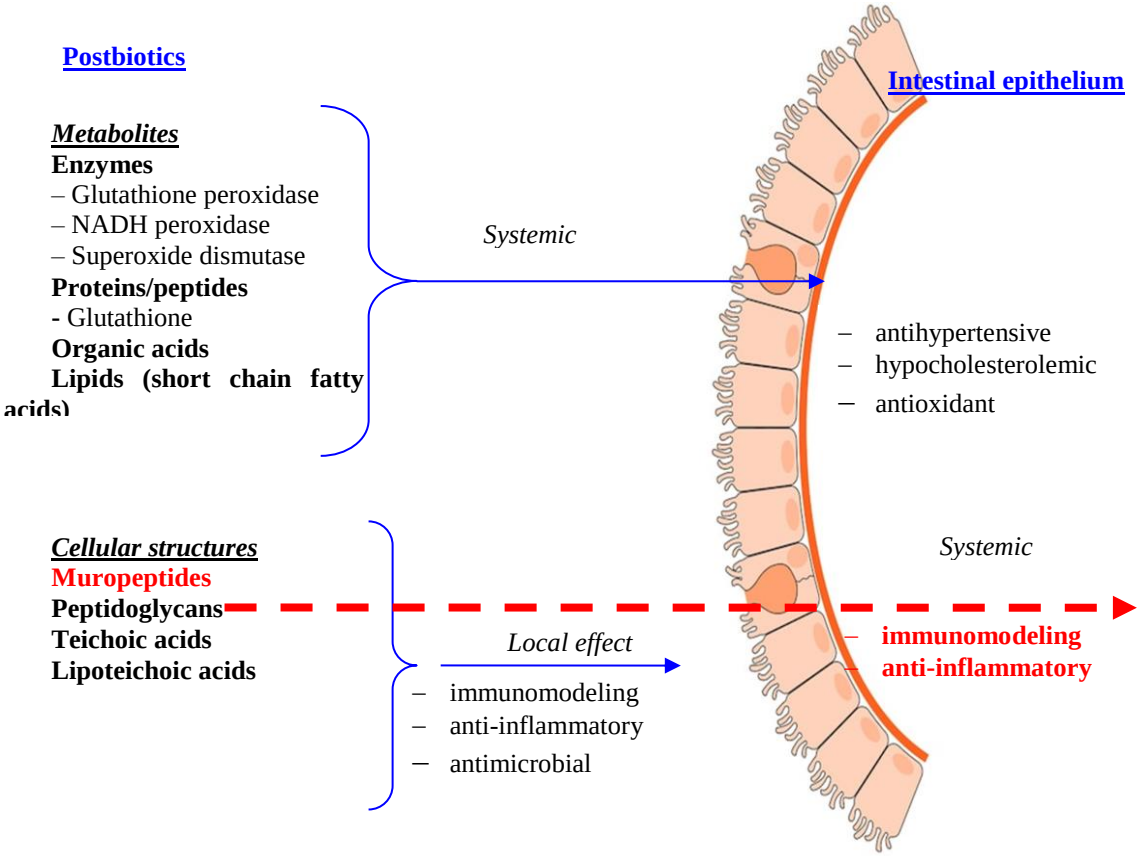

Fig. 3. Effect of postbiotics at the local and systemic level

Thus, muropeptides are the most studied PAMPs structures characterized by a pronounced immunostimulatory effect [71-73], and given the possibility of their transport through the intestine during enteric administration (Fig. 3), muropeptides are promising components of postbiotic origin for functional foods, the use of which is intended for the population with a reduced immune status.

Conclusion

Over the past few decades, the demand for functional foods has exploded worldwide. The production of functional foods and ingredients needs to be regulated at the state level. There is no harmonization in the definitions of functional foods and their classification at both the global and state levels. The term "functional food" is often absent in the legislative acts of countries that actively produce functional foods, and the term "health-related food" is used instead. As a rule, health-related foods are subject to quality and safety requirements that are identical to those of conventional food products. Exceptions are regulations that establish rules for labeling FFPs and statements regarding their physiological effects or the content of a particular ingredient that may affect physiological aspects. In Europe and the USA, much attention is paid to the safety of "health-related food" and the novel food products. European Food Safety Authority and the US Food and Drug Administration require sponsors to submit information on the composition of multiple batches of a product to support safety evaluations for novel foods GRAS ingredients. In Ukraine, the legal status of the terms "functional food product" and dietary supplement was regulated by Law of Ukraine 771 "On Basic Principles and Requirements for Food Safety and Quality", but in the version of this law dated 16.01.2020, this term was excluded, the term "dietary supplement" was edited and the term "novel food product or ingredient" was included, which is related to the process of harmonization of Ukrainian and European legislation in the food sector. In 2020, the Ministry of Health of Ukraine approved Order No. 1145 "On Approval of the Requirements for Nutrition Claims and Health Claims for Food Products", which regulates the following concepts: claims and conditions for their use; health claims allowed to be used in food labeling and advertising, except for claims about reducing the risk of diseases and claims related to the development and health of children; claims about reducing the risk of diseases and claims related to the development and health of children. Unfortunately, Ukrainian regulations do not contain claims and conditions for the use of claims about pro- and prebiotics that have GRAS status worldwide. Particular attention should be paid to the possibility of using postbiotics as functional food ingredients with immunological activity.

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РЕГУЛЮВАННЯ ФУНКЦІОНАЛЬНИХ ХАРЧОВИХ ПРОДУКТІВ В УКРАЇНІ ТА СВІТІ. ПЕРСПЕКТИВИ ВИКОРИСТАННЯ ПОСТБІОТИКІВ ЯК ФУНКЦІОНАЛЬНИХ ІНГРЕДІЄНТІВ

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Анотація. Функціональне харчування дозволяє індивідуалізувати особливості та потреби кожної людини. За останні декілька десятиліть попит на продукти, що позитивно впливають на здоров'я людини вибухнув у всьому світі. Ринок функціональних харчових продуктів у розвинених країнах оцінюється в 300 млрд $ США, це обумовлює інвестиційну привабливість у дану сферу. Відповідно, виробництво функціональних харчових продуктів та інгредієнтів потребує урегулювання на державному рівні. Гармонізація у визначеннях понятть про функціональні харчові продукти та їхньої класифікації відсутня як на світовому, так і на державному рівнях. Не зважаючи на те, що поняття та термінологія функціонального харчування та засобів його досягнення є усталеним, у законодавчих актах країн, які активно провадять виробництво функціональних продуктів термін «функціоальний харчовий продукт» відсутній, натомість вживається термін «health-related food». Як правило, до «health-related food» висуваються вимоги щодо якості та безпечності, які є тотожними до вимог звичайної харчової продукції. Виключенням є нормативні документи, які встановлюють правила маркування функціональних харчових продуктів та твердження щодо їхньої фізіологічної дії, або вмісту того, чи іншого інгредієнту, що може впливати на фізіологічні аспекти. У Європі та США велика увага приділяється безпеці «health-related food» та новітніх харчових продутів. Європейське агентство з безпеки харчових продуктів і Управління з контролю за продуктами й ліками США вимагають від спонсорів надати інформацію про склад кількох партій продукту для підтримки оцінки безпеки для нових харчових продуктів і загальновизнаних безпечних (GRAS) інгредієнтів. В Україні юридичний статус понять ФХП, дієтична добавка регулювалась законом України 771 «Про основні принципи та вимоги до безпечності та якості харчових продуктів», але в редакції даного закону від 16.01.2020 цей термін було виключено, редаговано термін «дієтична добавка» та включено термін «новітній харчовий продукт чи інгредієнт», що пов’язано з процесом гармонізації українського та європейського законодавства у харчовій сфері. У 2020 році Міністерство охорони здоров’я України затвердило Наказ № 1145 «Про затвердження Вимог до тверджень про поживну цінність та заяв про користь для здоров'я харчових продуктів», який регулює наступні поняття: твердження та умови їх використання; твердження про користь для здоров’я, дозволені для використання у маркуванні та рекламі харчових продуктів, крім тверджень про зниження ризику виникнення захворювань та тверджень, що стосуються розвитку і здоров’я дітей; твердження про зниження ризику виникнення захворювань та твердження, що стосуються розвитку і здоров'я дітей. На жаль, українські нормативні документи не містять вимог та умов використання тверджень про про- та пребіотики, які мають статус GRAS у всьому світі. Особливу увагу слід звернути на можливість використання постбіотиків як функціональних харчових інгредієнтів з імунологічною активністю.

Ключові слова: функціональні харчові продукти, інгредієнти, нормативне регулювання, твердження, постбіотики, безпека.