

## ANTIMICROBIAL SUBSTANCES OF LACTIC BACTERIA AND PRACTICAL ASPECTS OF THEIR USE

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## АНТИМИКРОБНЫЕ ВЕЩЕСТВА МОЛОЧНОКИСЛЫХ БАКТЕРИЙ И ПРАКТИЧЕСКИЕ АСПЕКТЫ ИХ ИСПОЛЬЗОВАНИЯ

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## SUT KISLOTASI BAKTERIYALARINING MIKROBLARGA QARSHI MODDALARI VA ULARDAN FOYDALANISHNING AMALIY JIHTLARI

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**Relevance of the study.** Colonization of microorganisms in the intestines of a newborn child begins with bacteria entering the body of the baby with the first portions of mother's milk. Lactic acid bacteria (LAB), which are part of the intestinal microflora, are a large group of aerotolerant gram-positive microorganisms. This group of bacteria has been known to mankind since ancient times - even then, the positive effect of dairy products on human health was noted. Currently, LABs are used not only to expand the range of dairy products, but also to increase the shelf life of food products due to the formation of organic acids formed during the fermentation of sugars. The result of lactic acid fermentation is the rapid acidification of the environment and the associated inhibition of other groups of microorganisms. With the development of physicochemical methods of analysis, it has been proven that some species and strains of such bacteria form a variety of antimicrobial substances that have a number of advantages over synthetic preservatives. Currently, the use of LAB and their metabolites with antibiotic properties is one of the actively developed alternative approaches to food preservation, including children's products.

**Keyword:** Lactic acid bacteria (LAB),  $\beta$ -methyllanthionine, bacteria, kefir, yogurt, Lactococcus, Streptococcus.

**Purpose of the study.** To study the spectrum and applied value of antimicrobial substances secreted by lactic acid bacteria.

**Materials and methods.** A literary review of domestic and foreign scientific publications was carried out.

**Results and discussion.** Attempts to influence the intestinal microbiome, and through it - on human health, have a long history associated with the name of the great Russian scientist, Nobel Prize winner I. I. Mechnikov, who in 1907 in his book "Etudes of Optimism" described the favorable role of bacteria in the preservation and maintenance of human health. On the example of lactobacilli, he developed the theoretical foundations of antagonism of microorganisms and their practical use. Subsequently, the antagonistic properties of lactic acid bacteria in relation to pathogenic microorganisms were studied by many researchers. These microorganisms in the process of development form organic acids from the carbon-containing components of the substrate, which drastically change the active acidity of the medium and thereby prevent the development of other types of microorganisms, including putrefactive and pathogenic ones. Therefore, this group of producers is of particular relevance for the development and production of children's food products, especially for medical purposes.

In Uzbekistan, the diet of young children traditionally contains various types of non-adapted fermented milk products. Their fundamental differences are in the quantitative and qualitative composition of starter cultures and the technological features of the preparation of the product, which together determine its final properties. Non-adapted fermented milk products for baby food (kefir, yogurt.) are allowed to be introduced into the diet of a child from 12 months.

Lactic acid bacteria, which form the basis of the starter microflora of dairy food products, are able to suppress the growth of a number of pathogenic and opportunistic microorganisms. The bactericidal properties of *Lactobacillus acidophilus* are due to the presence of specific antibiotic substances, the action of which enhances the combined presence of lactic, acetic and propionic acids. Numerous studies have shown that the antimicrobial effect of LAB is not limited to acidification of the environment - a significant role in the process of antagonism and inhibition of the growth of other members of the consortium belongs to the active synthesis and release of a whole complex of substances with fungicidal and bactericidal action.

A group of International Classification of Disease metabolites such as bacteriocins has been well studied.

One of the main reasons for the increased interest in the study of these substances is consumer demand for food quality and health safety, since widely used chemical preservatives and some antibiotics that increase the shelf life of food are of great concern to both scientists and consumers.

Bacteriocins are antibacterial substances of a protein nature produced by bacteria and suppress the vital activity of other strains of the same species or related species.

These substances are a complex of peptides with a molecular weight of 2 to 35 kDa, which differ significantly from each other in terms of physicochemical characteristics and biological effects. Bacteriocins are synthesized by almost all known bacteria, including lactic acid ones. The synthesis of bacteriocins is a genetically determined feature of microorganisms, which manifests itself in the fact that each strain is able to form one or more specific, strictly specific antibiotic substances. In most populations of lactococci, the synthesis of bacteriocins can be induced by genetic engineering methods, various physicochemical influences:

ultraviolet rays, chemical mutagens, DNA tropic substances, peroxides and other agents.

The biosynthesis of bacteriocins, as well as other biologically active substances, is influenced by the cultivation conditions of the producer: the composition of the nutrient medium, pH, temperature, and incubation time. It is assumed that the mechanism of the biological action of a number of bacteriocins is associated with a violation of the permeability of cytoplasmic membranes. Increasing evidence suggests that bacteriocins differ in structure, mechanism of action, biosynthetic pathways, and gene regulation [7]. Bacteriocins are regarded as effective preservatives in the food and pharmaceutical industries to prevent food spoilage and the development of pathogenic bacteria. In addition, elucidation of the mechanisms and features of their biosynthesis has led to the practical use of bacteriocin-controlled gene expression systems and biosynthetic enzymes of lantibiotics of the bacteriocin class as tools for the development of new peptides. Bacteriocins belong to a special group of antimicrobial substances called lantibiotics.

Lantibiotics are polycyclic antibacterial peptides, which include such thioether amino acids as lanthionine and  $\beta$ -methylanthionine [2; eleven]. These substances have a wide antimicrobial spectrum of action.

Lantibiotics are promising candidates for the treatment of certain infections, such as those caused by *C. difficile*. This is due to their mechanism of action, which is believed to reduce the possibility of developing resistance to the antimicrobial agent used. Their use is also supported by the fact that they often have a less harmful effect on the normal intestinal microbiota compared to traditionally used antibiotics [9]. The possibility of using bioengineering methods to obtain even more effective modifications of lantibiotics is also important.

Nisin is one of the well-studied lantibiotics. Nisin is a 34 amino acid lantibiotic produced by representatives of the genera *Lactococcus* and *Streptococcus*.

Over the past few decades, nisin has been widely used as a registered food additive - preservative E234. Since then, many natural and genetically modified variants of nisin have been identified and studied with unique antimicrobial properties. Nisin is

considered a safe peptide with a studied potential for clinical use, and therefore, over the past two decades, its use has been extended to biomedical fields [10].

Studies have shown that nisin can prevent the development of drug-resistant bacterial strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) [1], pneumococci, enterococci and *Clostridium difficile* [10]. Nisin has now been shown to have antimicrobial activity against both gram-positive and gram-negative pathogens that cause infectious diseases. Nisin exhibits biofilm inhibiting properties and may work synergistically when combined with conventional drugs. In addition, nisin may activate the adaptive immune response and play an immunomodulatory role. Some evidence indicates that nisin can influence tumor growth and exhibit selective cytotoxicity against cancer cells [4].

At the same time, it should be noted that the spectrum of nonspecific antimicrobial substances produced by LAB under different conditions is very diverse, it is represented not only by nisin and has inhibitory properties against different groups of bacteria. Thus, some scientists have noted an antagonistic effect against *Staphylococcus aureus* due to the formation of hydrogen peroxide during the development of KSD in the presence of atmospheric oxygen [3]; synthesis of pyrrolidone-5-carboxylic acid by some subspecies of *Lactobacillus casei* and associated suppression of *Bacillus subtilis* hay bacillus [8]; inhibition of a whole group of gram-negative pathogenic bacteria of the genera *Salmonella*, *Yersinia*, *Escherichia* and *Aeromonas* as a result of the action of diacetyl [cit. according to: 13].

Many scientists have noted the positive effect of reuterin, produced during the anaerobic metabolism of glycerol, in suppressing the growth of the fungus *Penicillium expansum*, as well as the pathogenic bacteria *Staphylococcus aureus*, *Salmonella enterica* ssp. *enterica*, *Listeria monocytogenes*, *Salmonella cholerae suis* ssp. *Cholerae suis*, *Yersinia enterocolitica* and many others [8, 6]. Interesting and encouraging data are shown in relation to the inhibition of such a microorganism as *Klebsiella pneumoniae*, which is the causative agent of hospital infections [12].

3-phenyllactate is one of the intermediate products of phenylalanine metabolism in LSD cells. This final metabolite exhibits proven antibiotic activity against gram-positive and gram-negative bacteria, and also acts on a wide range of microscopic fungi [13].

One of the currently actively studied compounds synthesized by LAB are diketopiperazines (cyclic dipeptides) - recent publications report their effectiveness against multiple drug-resistant gram-positive and gram-negative bacteria, human and plant pathogenic fungi, and influenza A (H3N2) virus. [five]. It is noteworthy that at this stage of research, the interests of scientists concern not only the nature of the action of these substances in relation to pathogens, but also the development of methods for isolation and purification - i.e. the scientific community is ready for the practical use

of this group of substances. The functions of lactic acid bacteria are diverse, including the release of antimicrobial substances that support the microflora of the gastrointestinal tract in both adults and children.

When preparing fermented milk products, from the moment the starter microorganism is introduced into dairy products, a chain of biochemical transformations of basic nutrients to their structural components is launched. Starter microorganisms secrete proteo and lipolytic enzymes, with the help of which milk proteins are partially hydrolyzed to peptides of various molecular weights and amino acids and milk fats to di-, monoglycerides and free fatty acids. Partial hydrolysis of proteins and fats facilitates the absorption of split components in the child's gastrointestinal tract.

It is important to note that the product of lactose metabolism - lactic acid - has a number of useful properties. For example, in fermented milk products, it is able to coagulate casein with the formation of a milk clot, and in the intestine, by lowering the pH of the medium, it creates unfavorable conditions for the vital activity of pathogenic microorganisms.

**Conclusions.** Thus, today it remains relevant to study the possibilities of practical use and expansion of the scope of individual antimicrobial substances secreted by lactic acid bacteria. No less important is the search for new yet unknown agents with antibiotic activity produced by this group of microorganisms. Undoubtedly, the high practical value of these studies is significant for the subsequent development of children's dairy products, especially for medicinal purposes.

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