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IMMUNOLOGICAL PROPERTIES OF THE BACTERIAL ORIGIN COMPOUNDS

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Abstract. It is shown that microorganisms are an integral element of the macroorganism immune system. Peptidoglycan, muramyldypeptyd, teichoic acids are structural components of cell walls of microorganisms. These components are an object for recognition of the innate immunity system. The necessity of the bacteria cell walls destruction with a view to obtain the immunotropic products for enteral consumption, able to overcome the intestinal barrier, was substantiated.

The use of lactic acid bacteria (ICD) for such purposes is perspective and safe, since the considerable experience of their cultivation was accumulated, in addition, ICD have got «GRAS» (Generally Recognized As Safe) status. Waste products of ICD are organic acids, hydrogen peroxide, bacteriocins and others. These substances have got antagonist activity, implicitly affect on the immune system, reducing the antigenic load caused by pathogenic microorganisms.

A number of physical, chemical and biochemical methods of bacteria cell walls destruction were considered. The priority methods is the soft influence, namely the use of specific enzymes or hydrolases, own autolyzins with a combination of physical destruction methods.

Keywords: immunotropic properties, bacterias, **teichoic acids**, peptidoglycan, muramildipeptyd, destruction, enzymes.

ІМУНОЛОГІЧНІ ВЛАСТИВОСТІ СПОЛУК БАКТЕРІАЛЬНОГО ПОХОДЖЕННЯ

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Анотація. Показано, що мікроорганізми є невід'ємною ланкою функціонування імунної системи макроорганізмів. Структурні компоненти клітинних стінок мікроорганізмів – пептидоглікани, мурамилдипептид, тейхоєві кислоти – є об'єктами для розпізнавання системою вродженого імунітету. Обґрунтовано необхідність деструкції клітинних стінок бактерій з метою отримання імунотропних продуктів для ентерального споживання, здатних подолати кишковий бар'єр.

Перспективним і безпечним для таких цілей є використання молочнокислих бактерій (МКБ), оскільки накопичено значний досвід їхнього культивування, до того ж, МКБ мають «GRAS» (Generally Recognized As Safe) статус. Продукти життєдіяльності МКБ – органічні кислоти, перекис водню, бактеріоцини та ін. – проявляють антагоністичну активність, опосередковано впливають на імунну систему, знижуючи антигенне навантаження, що викликається патогенними мікроорганізмами.

Розглянуто ряд фізико-хімічних і біохімічних способів руйнування клітинних стінок бактерій, при цьому пріоритетними є м'які методи впливу – використання специфічних ферментів-гідролаз або власних автолізинів з поєднанням фізичних методів деструкції.

Ключові слова: імунотропні властивості, бактерії, тейхоєві кислоти, пептидоглікани, мурамілдіпептиди, деструкція, ферменти.

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Introduction

The priority direction of development of modern society is taking the necessary measures to ensure the public health at the proper level. One of the causes of ill health and premature aging of the population is the low level of immunity. The man with the «low immunity» diagnosis is most vulnerable to colds, allergies, autoimmune diseases and other accompanying diseases.

One of the overcoming ways of these problems is the immunotropycal functional ingredients introduction into the diet. To immunocorrectors are carried immunostimulants, immunosuppressants and immunomodulators. The latter are the drugs that are capable to cause the multidirectional immune response. Immunomodulators are capable to raise or to lower the elevated reduced indicators of immune status. They are represented by microbial origin preparations, peptide nature, cytokines, immunoglobulins and others. In recent years, special attention is paid to immunomodulators of bacterial origin. These include degradation products of microorganisms cells and their metabolites [1-6].

Problem Analysis

The role of microorganisms in the human life is significant and diverse. The symbiotic relationships between macro- and microorganisms where appeared in the earliest stages of evolution and are the most important link in the formation of innate and adaptive immunity.

The bacteria in humans and animals are the main activators of the immune system. The full functioning of the immune system completely depends on the normal intestinal microflora, the respiratory tract, skin and others. It is generally known, that immune system of the sterile animals (gnotobionts) is atrophied, and they are vulnerable even before the opportunistic pathogens. The existence of innate immunity is based on the recognition of microbial ligands by receptors of immunocompetent cells. During of the evolution, the innate immune system mechanisms have got acquired the ability to recognize microorganisms pathogens in humans. During of the evolution, the innate immune system mechanisms have got acquired the ability to recognize microorganisms disease pathogens in humans [7-9].

As objects to recognize by innate immune system following bacterial structures are used: peptidoglycan; polysaccharides containing mannans; lipopolysaccharide; Specific structures based teichoic acids; N-formylmethyonin et al. (Fig. 1, Tab. 1) [9].

ient is ineffective. The intestinal epithelium is covered with mucus, antibacterial peptides and represents a complex biological filter, which controls introduction into an organism of microbial products that have an immunoregulatory effect [6,10-11].

Key molecular mechanism of immune system and normal microbiota interaction is recognition of the soluble microbial products by pattern recognition receptors. The signals for adaptive immune response starting are not living bacteria, but their fragments or metabolic products, which achieve the immune system cells, passing through the intestinal epithelium [10].

In this regard, it is appropriate directional partial destruction of bacterial cells with purpose of obtaining biologically active substances (BAS) that can easily be absorbed and enter into biochemical processes, accelerating the expected immunotropic effect.

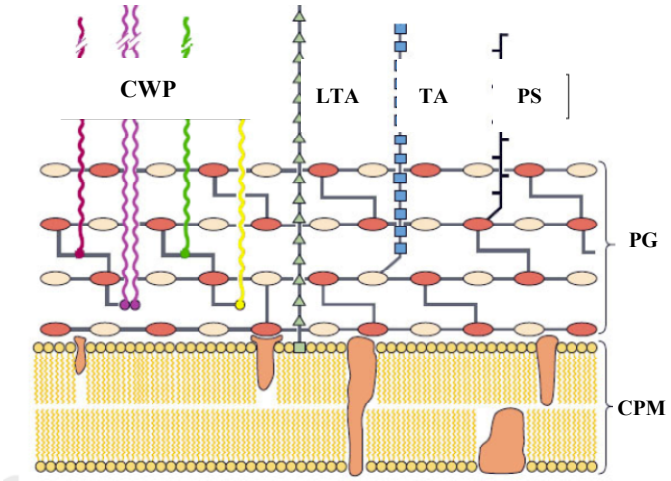

Fig.1. Staphylococcus cell wall: the interaction with the innate immune system: CPM – cytoplasmic membrane; PG – peptidoglycan; PS – a polysaccharide; TA – teichoic acid; LTA – lipoteichoic acid; CWP – cell wall proteins.

Table 1 – The characteristics of humoral receptors of immunocompetent molecules and their ligands

The target for recognition	Brief description, pro-inflammatory activity	Humoral receptor / effector
PG	It are contained in grampositive and gramnegative bacteria, induces the release of TNF-α, interleukins (IL) (IL-1β, IL-6, IL-10). It has a synergistic action with LTA	Lysozyme. Peptidoglycan-recognition protein
TA and LTA	It are contained in the most grampositive bacteria (50 % dry weight). It are considered as LPS analog of the induction of inflammation LTA and TA. It generates the TNF-α, IL-1, IL-6, IL-8, IL-12 and other inflammatory activator	Mannose binding protein. Fikolyns. Beta-lysine.
Lipopolysaccharides (LPS)	It are the structural components of the outer membrane of gram-negative bacteria. Inflammatory Activity caused lipid complex (lipid A). It induces the production of IL-1, IL-6, IL-8 and TNF-α	LPS-binding protein (LBP). Bactericidal / permeability-enhancing protein
Mannose	It is contained in gramnegative and grampositive bacteria, fungi and other microbes	Mannose binding protein.

Using whole microbial cell as a functional ingred

It is interesting to use for such purposes of lactic acid bacterias (LAB) because was accumulated significant experience of their cultivation for eubiotical, medicines and dietary supplements. In addition, the LAB have got «GRAS» (Generally Recognized As Safe) status, which defines them as absolutely safe for human health [3,5,10].

LAB are the representatives of the normal microflora and produce biologically active substances, which have got an antagonistic, immunomodulatory, antitumor activities [12-14].

Considerable importance in relation of the macroorganism immune status have got the antimicrobial metabolites produced by LAB. These substances improve the functional activity of mononuclear phagocytes, stimulate the macroorganism immune system.

The aim of the review is the representation of the detailed information about the immunotropic substances produced by the lactic acid bacteria and structural components of cell walls; a review producing methods of these biologically active substances.

The biologically active LAB metabolites

Are presently known various positive effects of lactic acid probiotic bacteria, confirmed by numerous clinical studies. First of all it should be noted that these bacteria have an important role in maintaining colonization resistance, that is, have pronounced antagonistic activity against pathogenic microorganisms. Such effects are due to by the fact that LAB produce the various organic acids, hydrogen peroxide, bacteriocins, short chain fatty acids, diacetyl [2-5,10].

The main end metabolites, formed by the LAB during of the fermentation are lactic and acetic acid. Active acid production is considered as one of the important factors of antagonism in regard to other types of bacteria. Acetic acid has a broader spectrum of antimicrobial activity as compared with lactic. At the same time, these acids in mixtures are showing synergistic effects and inhibit the growth of pathogenic Gram-negative bacteria *Salmonella typhimurium*. At a pH below 5.0, the lactic acid inhibits the growth of spore-forming bacteria. The lack of parallelism between the intensity of acid production and antagonistic activity of lactobacilli where noted in some studies [2,4].

In this regard, the formation of lactic acid is not regarded as the sole criterion for their antagonistic activity. Among antagonistically active bacteria strains are encountered weak acid producers and culture with a strong acid production can manifest themselves as weak antagonists [5].

An important role in the mechanisms of antimicrobial and virucidal activity of lactobacilli is their ability to produce hydrogen peroxide. Thus, the virusocidal effect of acidophilic lactobacilli in regard to human immunodeficiency virus (HIV type I) was detected [3]. Lactic acid bacteria are able to produce hydrogen peroxide, exhibit the antibacterial activity in regard to pathogenic and opportunistic pathogens.

The manifestation of the hydrogen peroxide bactericidal action against grampositive and gramnegative microorganisms, for example against the *Staphylococcus* and *Pseudomonas*, due to the strong oxidizing action in regard to the structure of microorganisms protein molecules. It exerts an inhibitory effect on the growth of bacteria catalase. Owing to the peroxides accumulation by *Lactococcus* and *Lactobacillus*, the *Staphylococcus aureus* and Gram-negative *Pseudomonas spp* inhibition was observed.

The ability of lactobacilli to produce hydrogen peroxide is regarded as the predominant factor in the mechanism of manifestation antagonistic activity as compared with the action of organic acids [2]. The synthesis of hydrogen peroxide highly virusocidal has a marked effect against the human immunodeficiency virus [4]. The synthesis of the highly active hydrogen peroxide has expressed virusocidal activity against human immunodeficiency virus [4].

Certain types of lactobacilli produce the diacetyl, which at a low pH are retarding the growth rate of *E. coli*, *Mycobacterium tuberculosis*, some grampositive bacteria.

All lactic acid fermentation microorganisms produce the antimicrobial protein nature substance. It is a bacteriocins. The bacteriocins are divided into 2 classes: lantibiotics (I class) and nelantibiotiki (II class) [5].

Lantibiotics is thermostable bacterial polypeptides weight from 3 to 7 kDa, which include rare thioether amino acids such as lanthionine and methyllanthionine. These substances have got a wide spectrum of antimicrobial action.

Class II bacteriocins are classified into several groups: microcins – thermostable low molecular weight peptides 1.0 – 2.0 kDa, high molecular weight thermolabile proteins 10 – 5000 kDa and protein complexes. For the last antimicrobial functions manifestation is needed carbohydrate or lipid components [5,10].

The bacteriocins are secreted by lactic acid bacteria, often have a narrow activity spectrum, which is compensated by the ability of these microorganisms to synthesize several antimicrobial substances belonging to different classes and having a different activity spectrum.

On target-bacteria recognition the LAB bacteriocins are divided into two groups. The representatives of the first group are characterized by a narrow spectrum antibacterial action. They cause the death of organisms, similar to the producer organism.

This group includes laktotsin B and F 27, amilovorin, pediocin N 5P, tepmofilin A, kurvatsin A, amilovorin L 471, enterokoktsin [5]. Belonging to the second group bacteriocins inhibits the growth of many species of gram positive microorganisms, including *Listeria monocytogenes, Clostridium botulinum, Clostridium sporogenes, Staphylococcus aureus, Pediococcus acidilactici, Bacillus spp., Enterococcus faecalis*. The second bacteriocins group are included pediocin A, atsidotsin B, diacetin B 1, kurvatsin FS 47, lacticin 3147, plantaritsin C, enterokoktsin, salivaricin, nisin, sarkatsin 674, mutatsin [14-15].

Immunotropic components of LAB cell wall

Biogeteropolimer peptidoglycan (PG) is composed of long chains of glycans. Peptidoglycan backbone of the molecule is a disaccharide. It is formed by N-acetyl-glucosamine and N-acetylmuramic acid, connected by glycosidic bonds. The oligopeptides are attached to the N-acetylmuramic acid molecule and form a side chains. Binding peptidoglycan fragments lies in the formation of a peptide bond between the terminal amino acid residue of the bridge (D-alanine) from the penultimate amino acid residue adjacent bridge (L-lysine or diaminopimelic acid in bacteria depending on the species). It was founded more than 100 different chemical types of peptidoglycan in the composition of Gram-positive bacteria. Two particular of peptide tail are deserving the attention: the presence of amino acids in the D-form (unnatural configuration) and a high content of amino acids with two amino groups. Both amino groups of these amino acids can be involved in the formation of peptide bonds, and the second amino group can be involved in the formation of additional bonds between peptide chains heteropolymer. In most cases, the peptide bond formation are conditioned by linking of the carboxyl group of D-alanine of first tetrapeptide and the free diaminopimelic acid amino group of the second tetrapeptide. Sometimes, the connection between the tripeptides of the various glycan chains are carried by means of other amino acids [7-8, 16-15].

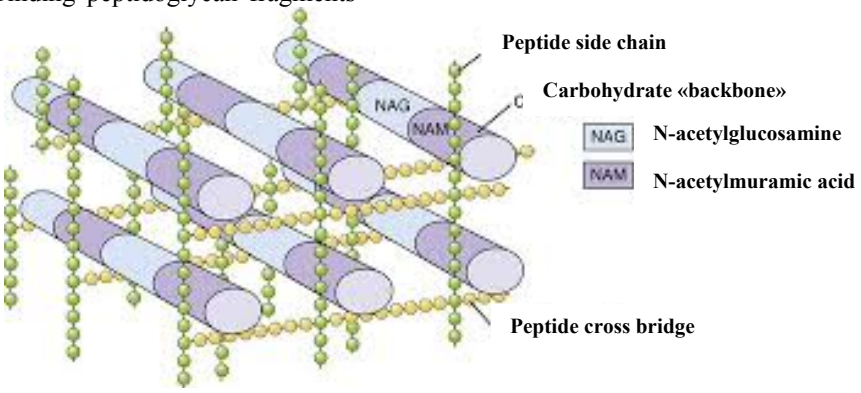

Fig. 2. A peptidoglycan molecule fragment of the grampositive bacteria cell wall

The PG of grampositive bacteria is an essential element of the cell wall, providing its strength, receptor and other functions. Violation of these functions leads to a microbial death. Therefore, PG is an attractive target for the detection of gram-positive (and to a lesser degree of Gram negative) bacteria and their destruction. Widely known the protective recognizing and lysing PG enzymes. These are included lysozyme, PG-recognizing blood protein (PG-amidase). Signal detection of peptidoglycan and specific enzymes that destroy the AI are shown in Figure 3

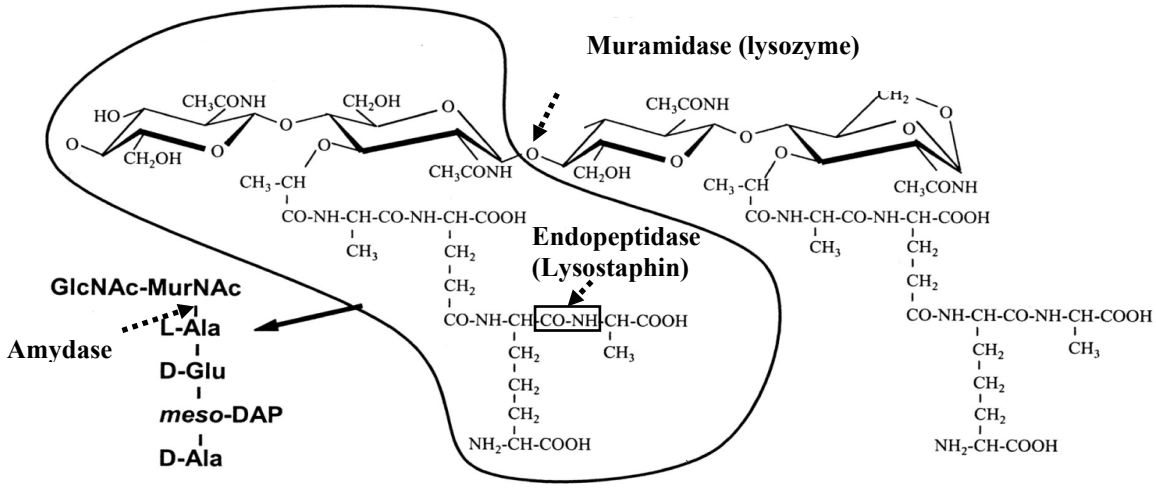

Fig. 3. A signal peptidoglycan detection [8]

After the interaction with effector humoral receptors the cleaved PG is transported into cells and is recognized by cytoplasmic receptors (proteins Nod 1 and Nod 2). To same consequences leads the autolysis of bacteria, as well as the Staphylococcus uptake and digestion by phagocytes, transcytosis or intracellular multiplication of parasite. The structures that are recognized by proteins and Nod1 Nod2 are shown in Figure 4.

The minimal structural unit of peptidoglycan, recognizable by intracellular Nod 2 receptors is muramyl dipeptide (MDP) (Fig. 5).

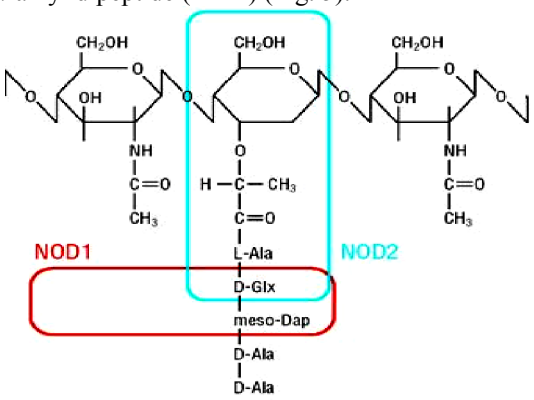

Figure 4. The structures recognized by Nod1 and Nod2 proteins [7]

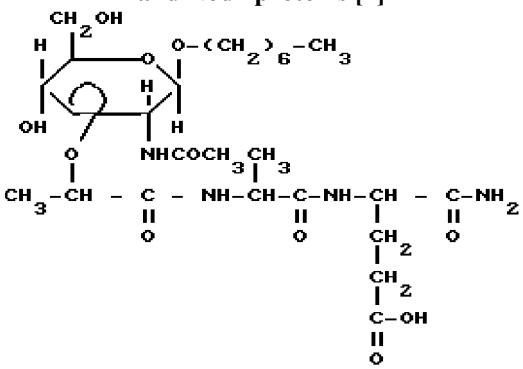

Fig. 5. MDP structure

Start of studies on MDP and its derivatives, laid as early in 1974. French researchers under the leadership of E. Lederer proved that exactly MDP, incoming in the structure of the mycobacterial cell wall, cause an immunostimulatory and adjuvant effects, stimulate an antimicrobial activity, antitumor immunity, activate the immunocompetent cells and induce the synthesis of several cytokines [15].

It is now established that the MDP has all the necessary properties for the pathogen-associated molecular patterns (Pathogen-Associated Molecular Patterns, PAMPs), expressed in the stimulation of innate immunity and the ability to form a protection against microbial pathogens in vertebrates [7-8].

MDP host initiates a signal a cascade of reactions that leads to the synthesis of pro-inflammatory cytokines by immunocompetent cells and activation of immunological defense mechanisms of the organism.

Muramyl peptides constantly get in an animals and humans organism as a result of the bacteria cell wall degradation and found in many tissues at low concentrations providing a variety of neuro- and immunoregulatory effects. Exogenous administration of derivatives MDP reproduces physiological and evolutionary enshrined modulation of the immune response mechanisms [17-23].

Teichoic acid (TC). In the last decades, special attention of researchers from different countries are attracted on the cell wall components of lactic acid bacteria, among which a special place is taken by teichoic acid.

From the literature it is known, that these biopolymers can influence on the cellular tissue, immune system of warm-blooded animals and humans, as well as participate in many biological processes, including adhesion, the pathogenesis of some diseases [24]. Particular interest is caused the teichoic acids probiotic bacteria, their functional role and ability to interact with receptors of eucaryotic cells. The TC are an integral part of the cell wall and thus are in close contact with the all processes, taking place in its participation. These are included the growth and division of cells, the binding and redundancy of cations, which are necessary for the functioning of membrane enzymes, intercellular recognition processes, phages reception, pathogenicity. The teichoic acids and other anionic compounds of the cell wall, are contribute significantly to the formation of a polyelectrolyte gel structure and determine its mechanical properties [25]. Together with other components of cell wall teichoic acids are responsible for cell sensitivity to several antibiotics and bacteria immunomodulatory properties [25-27]. Teichoic acid, peptidoglycan and the like, part of the cell wall of Gram-positive eubacteria. TC are polymers that are based on ribitol (five-atom alcohol) or glycerin (triatomic alcohol), the remains of which are interconnected by phosphodiester bonds. Some of the free hydroxyl groups in alcohols molecules can be substituted with alanine residues of D-glucose, N-acetylglucosamine and other sugars (Fig. 6).

The teichoic acids can be coupled covalently with the N-acetylmuramic acid. Question of the TC connection nature with the peptidoglycan (PG) was raised back in 1963. Even then it was assumed that this connection is covalent, as indicated by lower TC rate of extraction from the cell wall using TCA or alkali. The studying of PG enzymatic degradation products allowed to conclude that the TC is probably are attached to PG in a phosphodiester form through a terminal phosphate group to the C-6 muramic acid residue. Phosphodiester bond initially regarded as the only connecting link, but later found out that TC is connected to PG through the so-called "binder oligomer", which is a mandatory component of the glycerol phosphate. Wide dissemination and a huge variety of LC in the gram-positive bacteria cell walls, certainly, point to the importance of these natural compounds in cell vital functions [24]. Even under

unfavorable growth conditions, when the only vital compounds are synthesized, TK synthesis proceeds in full.

The anionic polymers of the cell walls perform a number of functions. Their ability to bind cations may protect the cells from the toxic metals effects and provide the necessary divalent cations reserve such as magnesium [24]. It is also shown the interaction between the main autolyzin N-acetyl-L-alanine amidase and TC in some bacteria, leading to the activation of the enzyme. The covalently linked TC with PG make an electrolyte gel, forming overall charge cell surface and providing passage of many processes and biochemical reactions in the cell wall [27]. TC have got an immunological and adhesive properties and they are participate of the bacteriophages reception. Their role in bacterial aggregation and determination of the pathogenic properties of certain microorganisms was shown also.

Since this is a long linear molecules, they can penetrate the whole layer of peptidoglycan, reaching the outer surface of the cell wall. In this case, perhaps, they are major antigens of the gram-positive eubacterias. The remaining free phosphoric acid hydroxyls impart the polyanion properties of the teichoic acid. As polyanions, teichoic acids determine the surface charge of the cell. The sugar components of the teichoic acid are part of some bacteriophage receptors and define the ability of phage adsorption on the cell surface.

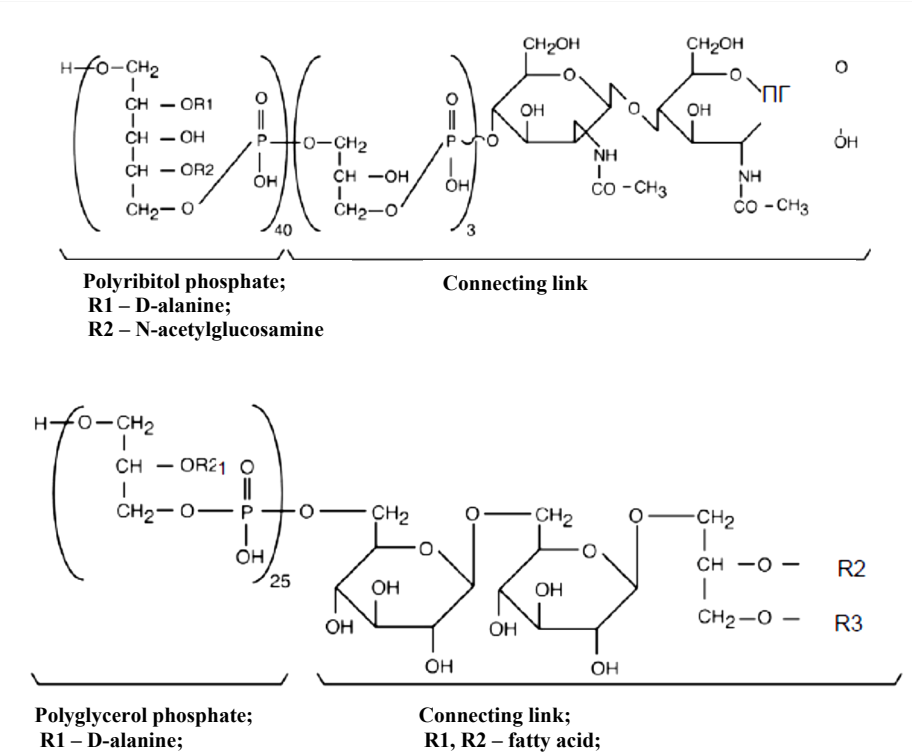

Fig. 6. The general structure of teichoic acids [7]

Teichoic acids are recognized by TLR 2 and 4 (Toll-like receptor), CD 14 receptor, CD 36. It are enhancing the signaling process upon stimulated TLR [7-8].

Producing methods of microbial structural components

The microorganism structural components are obtained by disintegration of their cell walls, using physical, chemical or combined techniques [28-29].

The physical disintegration methods are included sonication, rotating blades or vibrators, shaking with glass beads, punching through a narrow orifice under pressure, crushing the frozen cell mass, grinding in a mortar, osmotic shock, freeze-thawing, decompression (compression followed by rapid pressure reduction), the effect of high temperatures, microwave processing. Physical methods for the cells destruction are more economical than chemical and enzymatic. At the same time, these methods of cell disintegration inherent non-selectivity: processing may affect on the quality of the resulting product [28-35].

Chemical and enzymatic methods are more selective. Cells can be disrupted by toluene or butanol, acid, alkali, antibiotics, enzymes. Autolysis of cells can be performed at the specific substrate limitation, or lysis when bacteriophage infecting. Most bacteria synthesize a group of enzymes known as autolysins. It are capable to hydrolyze the own peptidoglycan of the cell wall [3,10]. Autolyzins are localized on the outer membrane surface, but in the logarithmic growth phase they are linked to the cell wall. Autolyzins are universal enzymes of bacteria, containing PG. According to the mechanism of action, autolyzins are divided into three main groups: glucosidase (N-atsetilmuramidazy) destroys the glycosidic bonds in the bark

of glycan chains: endo-N-β-atsetilmuramidaza – between the N-acetylmuramic acid, N-acetylglucosamine and endo-N-β-atsetilglyukozamidaza – between N-acetylglucosamine and N-acetylmuramic acid; N-acetyl-L-alaninamidaza hydrolyzes the bond between the carboxyl group of lactic acid and the amino group of L-alanine; several endopeptidase types destroy peptide bonds in the peptide subunits (Fig. 7).

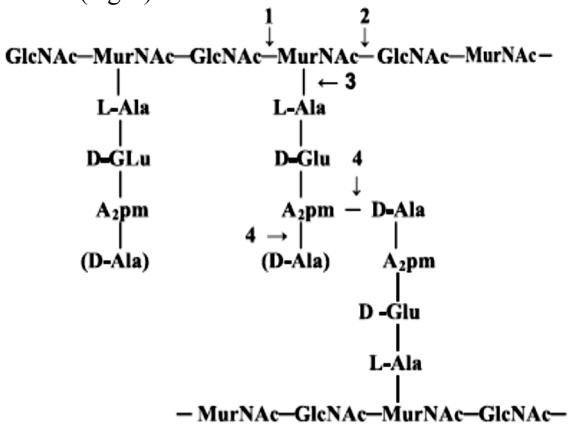

Fig. 7. The peptidoglycan degradation scheme by specific autolyzins: N-atsetilglyukozamidase (1), N-atsetilmuramidase (2), L-alaninamidase (3), endopeptidase (4) [7].

In practical terms, the physical disintegration methods of the bacteria cell walls in conjunction with chemical or enzymatic methods advantageously are used.

Among the chemical methods the acid and alkaline hydrolysis are secreted. However, alkaline hydrolysis can not be used for the hydrolysis of the bacterial mass, in view of the fact that racemization occurs of most amino acids, and degradation of lysine, which is part of the peptidoglycan. Acid hydrolysis is carried, advantageously with mineral acids at elevated temperatures. An attractive aspect of acid hydrolysis is possible to obtain hydrolysates in a short time. Another positive aspect is the formation of bactericidal conditions during the process to prevent microbial contamination and to store hydrolyzate without preservation for a long time.

However, acid hydrolysis has also the negative sides – part of amino acids is destroyed under its influencet. It can be accompanied by the formation of volatile compounds. There is evidences in the literature, that at the acid hydrolysis the low molecular weight peptides (which is the TIR al.) with terminal structural deformation are produced, whereby they are not recognized by the cell receptors [6,11]. At the acid proteins hydrolysis, besides the peptide bonds gap the, the various associated reactions occur. Thus, the dipeptides, may to form a cyclic form, and upon the cycle cleavage to form the dipeptide with a reverse arrangement of amino acid residues. In addition, acid neutralization at the end of hydrolysis leads to the formation of high salt concentrations. And increasing of the anions concentration in some cases can to serve as factor toxicity.

Enzymatic hydrolysis methods are more lenient and sparing in comparison with the chemical. Hydrolysis is carried out in pH zones, corresponding to maximum enzyme activity, usually in a neutral, weakly alkaline or weakly acid medium. Optimum temperature corresponds, usually 35 – 50 °C. Enzymes, as opposed to acids and alkalis, act only on certain groups of compounds [28].

For the peptidoglycan destruction of bacterial cell walls is expedient to use the proteolytic enzymes, which are to cleave the peptide bonds in its structure. Another enzyme that actively hydrolyze bacterial cell is a lysozyme, on this, in fact, its antibacterial action is based. It catalyzes the hydrolysis of β- (1 → 4) glycosidic bonds between N-acetylglucosamine and N-acetylmuramic acid.

For example, in [29] *Lactobacillus bulgaricus* hydrolysis was carried by sequential treatment with pepsin, lysozyme and sonication.

Hydrolyzate of the lactic acid bacteria strain *L. acidophilus* B 2505 was obtained with the thermoacid hydrolysis method, which was the basis for the creation of «Biolakton» drug [30].

There is also a way of drug production [31], containing glycopeptides, that includes cultivating of *L. bulgaricus* biomass in special nutrient media (peptone or soy extract, yeast extract, glucose, etc.); trypsin treatment of biomass, biomass disintegration with ultrasound, the repeated biomass treatment with pepsin and trypsin, centrifugation, hydrolyze with lysozyme, chromatography.

In [32,33], for obtaining glycopeptides and other biologically active substances on the basis of lactic acid bacteria, was proposed the complex treatment of raw material. It involves the biomass preparation by the fermentation on culture medium; treatment the culture liquid acidic with the proteolytic enzymes, especially bromelain or pepsin; separation of lactic acid whey by ultrafiltration; by consistent sonication biomass or freeze-defrost, by boiling, by lysozyme hydrolysis; by separation suspension lysozyme hydrolyzate on a water-soluble mixture of glycopeptides and insoluble residue containing glycopeptides.

After cell disintegration is carried isolation of desired products. The literature analysis points to three main methods for the isolation of the metabolites and cellular fractions of microorganisms: centrifugation or sedimentation followed by separation of the supernatant, ultra-filtration, which allows to divide the low and high molecular weight substances.

Obtained active compounds are subjected, usually by adsorption cleaning for obtaining the highly purified target products. Since the molecules are contented the functional groups, informing them acidic or basic nature, it is usually used for this purpose by the ion exchange method to ion exchangers obtained

cellulose: acid cation CMC (carboxymethylcellulose) and DEAE anion exchanger. In recent years, the number of different ion exchangers greatly increased, and it is possible to choose the best for a particular substance. Among the ion exchangers, received sufficiently widespread, it should be noted, such as processed starch, dextran Sephadex, polymethacrylic cation exchanger, polyvinyl alcohol acid anion exchangers and others. To obtain a more highly purified target products use such methods as dialysis, gel filtration, freezing, electrophoresis, affinity chromatography and others.

Conclusions

Thus, it is shown that microorganisms are an integral element of the macroorganism immune system. Peptidoglycan, muramyldypeptyd, teichoic acids are structural components of cell walls of microorganisms. These components are an object for recognition of the innate immunity system. The necessity of the bacteria cell walls destruction with a view to obtain the immunotropic products for enteral consumption, able to overcome the intestinal barrier, was substantiated.

The use of lactic acid bacteria (ICD) for such purposes is perspective and safe, since the considerable experience of their cultivation was accumulated, in addition, ICD have got «GRAS» (Generally Recognized As Safe) status. Waste products of ICD are organic acids, hydrogen peroxide, bacteriocins and others. These substances have got antagonist activity, implicitly affect on the immune system, reducing the antigenic load caused by pathogenic microorganisms.

A number of physical, chemical and biochemical methods of bacteria cell walls destruction were considered. The priority methods is the soft influence, namely the use of specific enzymes or hydrolases, own autolyzins with a combination of physical destruction methods.

Are also prospective studies of the immunotropic properties of compositions, obtained by combining of LAB cell wall structural components and their metabolic products for use as functional food ingredients.

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ИММУНОЛОГИЧЕСКИЕ СВОЙСТВА СОЕДИНЕНИЙ БАКТЕРИАЛЬНОГО ПРОИСХОЖДЕНИЯ

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Аннотация. Показано, что микроорганизмы являются неотъемлемым звеном функционирования иммунной системы макроорганизмов. Структурные компоненты клеточных стенок микроорганизмов – пептидогликаны, мурамилдипептид, тейхоеви кислоты – являются объектами для распознавания системой врожденного иммунитета. Обоснована необходимость деструкции клеточных стенок бактерий с целью получения иммунотропных продуктов для энтерального потребления, способных преодолеть кишечный барьер.

Перспективным и безопасным для таких целей является использование молочнокислых бактерий (МКБ), поскольку накоплен значительный опыт их культивирования, к тому же, МКБ имеют «GRAS» (Generally Recognized As Safe) статус. Продукты жизнедеятельности МКБ – органические кислоты, перекись водорода, бактериоцины и др. – проявляют антагонистическую активность, опосредованно влияют на иммунную систему, снижая антигенную нагрузку, вызываемую патогенными микроорганизмами.

Рассмотрен ряд физико-химических и биохимических способов разрушения клеточных стенок бактерий, при этом приоритетными являются мягкие методы воздействия – использование специфических ферментов-гидролаз или собственных автолизинов с сочетанием физических методов деструкции.

Ключевые слова: иммунотропные свойства, бактерии, тейхоевые кислоты, пептидогликаны, мурамилдипептиды, деструкция, ферменты.

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