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REVIEWS

FUNDAMENTALS OF PROTEIN CHEMISTRY AT THE INSTITUTE OF BIOMEDICAL CHEMISTRY

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Eighty years ago, the Institute of Biomedical Chemistry (IBMC) initially known as the Institute of Biological and Medical Chemistry of the Academy of Sciences of the USSR was founded. During the first decades significant studies were performed; they not only contributed to a deeper understanding of biochemical processes in the living organisms, but also laid the foundation for further development of these fields. The main directions of IBMC were focused on studies of structures of enzymes (primarily various proteases), their substrates and inhibitors, the role of enzymes of carbohydrate metabolism in the development of pathologies, study of the mechanisms of hydrolytic and oxidative-hydrolytic transformation of organic compounds, studies of connective tissue proteins, including collagens, study of amino acid metabolism. It is difficult to find papers from that period in current online literature databases, so this review will help to understand the value of studies performed at IBMC during the first 40 years after its organization, as well as their impact on modern research.

Key words: enzymes; protein chemistry

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INTRODUCTION

In 2000, the Institute of Biomedical Chemistry was named after the outstanding Russian biochemist, Academician Vasily Nikolayevich Orekhovich, who headed the Institute of Biomedical Chemistry for 40 years, from 1949 to 1989. He laid the foundations of protein chemistry and the Russian school of proteolytic enzyme research. Over the last decades, his works were further expanded in the context of development and use of post-genomic high-throughput analytical methods for biosystems research and new analytical methods required to improve the concentration sensitivity of protein detection assays.

The traditions established at IBMC since its foundation — careful selection of personnel, use of the most advanced equipment, uniqueness of the chosen directions — are still relevant today. The review provides information on the results of landmark research of the IBMC scientists during the first decades after the Institute foundation. Although publications of this period are poorly represented in modern databases of literature sources, this does not reduce their importance. Results accumulated by IBMC scientists during well-planned and carefully performed experiments, their comprehensive analysis and clear data presentation may be considered as the basis of modern protein chemistry, despite the fact that they were obtained more than half a century ago.

1. PROTEASES, PEPTIDASES, AND OTHER ENZYMES

Since IBMC foundation, enzymes, their primary structure, structure of active cites, methods of enzymes activation, as well as their possible substrates and reaction products were actively studied at this Institute.

A significant part of V.N. Orekhovich's scientific research is related to the study of biochemical problems of embryogenesis, malignant growth, and tissue regeneration. His first experimental work was published in 1933 in the first issue of the first volume of the journal Doklady Akademii Nauk SSSR [1]. It was entitled “To the problem on activation of proteolysis in regenerating tissues”. V.N. Orekhovich investigated the intensity of proteolysis at different stages of tissue regeneration. An increase in the activity of proteolytic enzymes was observed not only in the actively growing part of the regenerate, but also in the tissues of the amputated organ. Studying the problem of malignant growth, V.N. Orekhovich convincingly demonstrated that tumor proteolytic enzymes preferentially cleaved proteins of the same animal species. Proteins of other animal species were either resistant to proteolysis or were cleaved very weakly by the enzymes of the particular tumor. The results of the work were widely published in our country and abroad. During the period from 1933 to 1945 V.N. Orekhovich published about 25 articles devoted to the problems of malignant growth, embryogenesis, and tissue regeneration.

The role of proteases and regulators of their activity, the significance of their destructive and regulatory functions in the process of carcinogenesis are currently studied in hundreds of laboratories worldwide [2–5].

The Laboratory of Biochemistry and Chemical Pathology of Proteins, headed by V.N. Orekhovich, was one of the first in the world and the first in our country, which started to study tissue proteases. Cathepsins (A, B, D, H, L) and dipeptidyl aminopeptidase IV were isolated and characterized in the laboratory [6–8], and their role in the development of various pathological conditions was investigated in a number of works [9, 10].

In 1988, the Laboratory of Biochemistry and Chemical Pathology of Proteins was headed by a student of V.N. Orekhovich, Doctor of Biological Sciences, Professor Nina Ivanovna Solovyeva. Under her leadership the laboratory continued to investigate the role of tissue proteases and their regulators in carcinogenesis using clinical material and transformed cell lines.

The main research directions for this laboratory, now headed by Academician Andrey Valerievich Lisitsa, include: studies of the mechanisms of drug biotransformation and its regulation in cell lines of hepatocytic origin by using omics technologies, bioinformatics, and cell technologies; analysis of the influence of key genes of the embryonic differentiation (Hh) signaling pathway on the expression of matrix metalloproteinases (MMPs) in cervical carcinoma. Thus, statement of scientific problems by V.N. Orekhovich has not lost its relevance to date.

1.1. Gastrointestinal Tract Enzymes

Pepsin is one of the first enzymes studied in the laboratory under V.N. Orekhovich leadership [11–13]. The study of the pepsin active site structure revealed that its activation involved hydrolysis of the N-terminal peptide fragment [14–16]. This stimulated studies of primary and spatial structure of pepsin in our country. Further work continued at the Institute of Bioorganic Chemistry of the Russian Academy of Sciences and the Institute of Molecular Biology of the Russian Academy of Sciences. They led to elucidation of the three-dimensional structure of pepsin and significant progress in understanding of the mechanism of its action (Dr. N.S. Andreeva, Corresponding Member of the Russian Academy of Sciences V.M. Stepanov, Dr. L.M. Ginodman).

Currently, pepsin and other preparations of gastrointestinal tract enzymes are widely used in conditions that are accompanied by the absence or deficiency of their own enzymes in the body. Enzyme replacement therapy is especially important in exocrine pancreatic insufficiency as well as lactase deficiency in infants. In addition, lactase is used in the food industry to create the currently popular lactose-free dairy products.

1.2. Enzymes of Carbohydrate Metabolism

Carbohydrates play an important metabolic role in the body; they simultaneously participate in energy and synthetic reactions of physiological and pathological processes: synthesis of DNA, RNA, intercellular matrix components, reduction of NAD and NADP, and also participate in the reactions of glycation and glycosylation of proteins.

The Laboratory of Biochemistry and Pathochemistry of Carbohydrate Metabolism headed by Professor Eugenia Lazarevna Rosenfeld specialized on studies of enzymes of carbohydrate metabolism and diseases associated with their deficiency. E.L. Rosenfeld and her colleagues isolated and characterized lysosomal acidic γ-amylase (α1,4-glycosidase) [17, 18], the enzyme involved in lysosomal glycogen breakdown. It was later found that a defect in this enzyme resulted in the development of a glycogen storage disease known as generalized glycogenosis type II (Pompe's disease). This disease is one of the few types of glycogenosis for which the recombinant enzyme is used as therapy, but its maximum effectiveness is observed only at the early stage of the disease. Therefore, certain attempts are now undertaken to apply gene therapy for the treatment of Pompe's disease [19]. In addition, other defects of carbohydrate metabolism [20] and related disorders have been investigated [21, 22].

Studies performed by E.L. Rosenfeld and her colleagues significantly influenced the development of prenatal diagnostics of carbohydrate metabolism diseases, and early detection of pathology and timely treatment.

1.3. Asparaginase

Asparaginase is an enzyme that cleaves the amino acid asparagine. Studies of this enzyme were carried out at IBMC in the Laboratory of Medical Enzymology headed by Academician Sergey Rufovich Mardashev. After the discovery of the antitumor effect of this enzyme on leukemia cells in mice, different bacterial asparaginases were studied and factors affecting asparaginase and glutaminase enzyme activities were identified [23, 24].

Since the enzyme has the potential to be used for the treatment of blood tumor diseases in humans [25, 26], asparaginase is still the object of research conducted in the Laboratory of Medical Biotechnology of IBMC initially headed by Professor N.N. Sokolov and currently by Dr D.D. Zhdanov.

The mechanism of cytostatic action of asparaginase is associated with hydrolysis of asparagine and reduction of its concentration in tumor cells, which need this amino acid for synthesis of proteins and nucleic acids. In contrast to healthy cells, tumor cells are unable to synthesize asparagine due to low activity of asparagine synthetase.

The main disadvantage of such chemotherapy is a possible allergic reaction to the bacterial enzyme used; therefore, methods are currently being developed to reduce immunogenicity, improve physicochemical properties of asparaginase, and increase the half-life [27, 28].

1.4. Kallikrein-Kinin and Renin-Angiotensin-Aldosterone Systems

During studies of the inflammatory process conducted at IBMC by Dr of Biological Sciences Tatiana Sergeevna Paskhina, a factor increasing vascular permeability was discovered. Later it was found that it was plasma kallikrein, an enzyme cleaving kininogens to bradykinin and kallidin [29], which increased vascular permeability. Subsequent studies were performed to investigate the ways of prekallikrein activation [30], the properties and the role of bradykinin and kallidin [31–35].

During the same period, another enzyme, carboxycathepsin (modern name — angiotensin converting enzyme, ACE), was isolated. This enzyme catalyzes two important reactions: it cleaves bradykinin and forms angiotensin II from angiotensin I [36, 37]. Thus, a more detailed study of the kallikrein-kinin system (KKS) and renin-angiotensin-aldosterone system (RAAS) and their role in the body, primarily in the regulation of vascular tone, began (Fig. 1).

It was already known that kallikrein-kinin and renin-angiotensin-aldosterone systems produced vasodilator and vasoconstrictor molecules, respectively, involved in blood pressure regulation. But in endothelial dysfunction, there is an increase in vascular tone, which leads to hypertension and worsening of other cardiovascular diseases, as well as pre-eclampsia in pregnant women and delayed fetal intrauterine development [40]. Therefore, studies on the search for ways to treat hypertension by ACE inhibition have been carried out [41, 42]. In a slightly different research context, such studies still continue at IBMC [43].

The role of KKS has now been shown not only in the regulation of vascular tone and pressure, but also in plasminogen activation, NO production, and inflammatory processes [44].

The functions of RAAS are determined by the balance of two pathways: canonical, which leads to the activation of angiotensin II by ACE and its effects, and non-canonical one, which involves ACE2 reducing the effects of angiotensin II. These pathways regulate blood pressure, water-salt balance, vascular permeability, oxidative stress, cell death and proliferation, proinflammatory and anti-inflammatory effects, angiogenesis, fibrosis, and hemostasis [45].

Besides its carboxypeptidase activity employed in the non-canonical RAAS pathway, ACE2 also acts as a receptor for the viral proteins of SARS-CoV-2 and SARS-CoV [46]. This interaction results in reduction of ACE2 activity and the protective effect of ACE2 in the non-canonical RAAS pathway is diminished, leading to lesions mainly in the lungs, heart, liver, and kidneys [47, 48].

2. COLLAGEN METABOLISM

Since 1945, the main research work of V.N. Orekhovich was focused on the study of the chemistry and biochemistry of connective tissue proteins. His studies of the collagen proteins, their

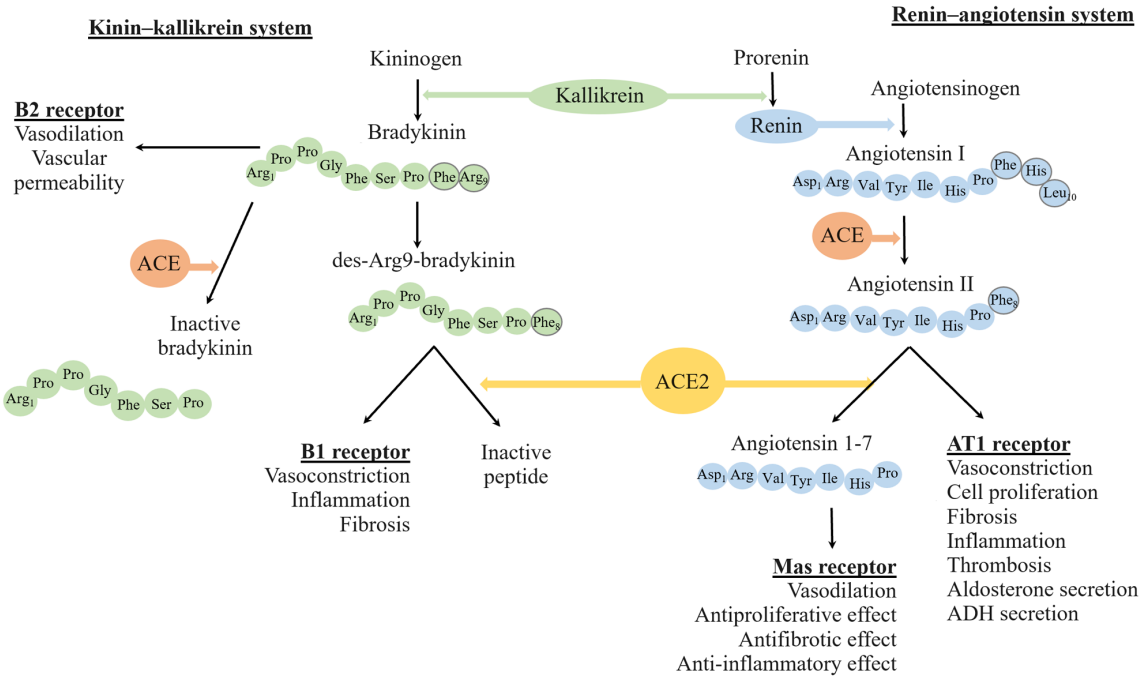

Figure 1. Relationship between the kallikrein-kinin (KKS) and the renin-angiotensin-aldosterone system (RAAS). Adapted from [38, 39].

physicochemical properties, chemical composition and structure, as well as the metabolism of these proteins under various normal physiologic and pathologic conditions made outstanding contribution in the field of protein chemistry. Collagens are a family of extracellular matrix proteins that account for 25–35% of the total protein mass. Collagens are a part of bones, cartilage, blood vessels, dentin of teeth, intervertebral discs, ligaments, lungs, etc. [50].

Interest in these proteins is associated with their involvement in physiological and pathological processes: growth and aging of the organism, hemostasis, reparative, inflammatory and tumor processes, and collagen diseases [51].

It should be noted that by 1947, not all the processes in which collagen was involved had been recognized and studied. V.N. Orekhovich and his team isolated procollagen (a protein unknown at that time) from animal skin [52]. Subsequent experiments provided convincing evidence that procollagen was a precursor of collagen [53, 54].

Since then, studies on the structure and role of collagen continued [55, 56]. It was shown that the lack of hydroxyproline and hydroxylysine significantly influenced the three-helix structure and stability of collagen [57]. Collagen was synthesized on endoplasmic reticulum ribosomes [58]. Collagen mRNA was isolated and translation of collagen peptides was reproduced in a cell-free system [59]. The interaction of collagen with fibronectin has been demonstrated [60]. Inhibition of procollagen and, consequently, collagen synthesis by cortisone (a steroid hormone of the adrenal cortex) has been shown [61]. The latter fact is important in the pathogenesis of hypercorticism, as well as in the treatment with steroidal anti-inflammatory drugs: prolonged increased concentration of steroid hormones inhibits collagen synthesis and causes development of steroid-induced osteoporosis.

Other causes that affect collagen biosynthesis, assembly, post-translational modification, secretion, and breakdown have now become known:

- more than 1000 collagen gene mutations leading to various diseases (Table 1) [62];
- autoimmune diseases (lupus erythematosus, rheumatoid arthritis).

The involvement of collagens in tumor progression, tissue repair, fibrosis development, as well as connective tissue diseases with a progressive course, leading to disability, reduced human performance, stimulate further research on collagens and their diseases. In addition, the study of the role of collagens in the process of skin aging has led to the active use of collagens and their hydrolysates in the cosmetic and food industries. In this context it is important to remember: when used superficially, collagen will not penetrate the skin because of its large size, and when taken through the gastrointestinal tract, it is hydrolyzed into individual amino acids, so it is not able to get into the skin in an unchanged form.

3. METABOLISM OF AMINO ACIDS AND THEIR DERIVATIVES

Amino acids are important molecules for synthesis of various compounds (proteins, enzymes, hormones, neurotransmitters, nucleotides, etc.) and the regulation of body functions [63]. Some specific reactions characteristic of amino acids were discovered and studied by scientists at IBMC. The scientific group headed by Academician Alexander Evseevich Braunstein discovered the process of transamination [64], actively studied the role of pyridoxal phosphate in the metabolism of tryptophan [65], cysteine [66–68], threonine [69]. In 1952, A.E. Braunstein together with M.M. Shemyakin proposed a theory of pyridoxal catalysis, summarizing all known reactions with this coenzyme in amino acid metabolism at that time, which contributed to the discovery of other reactions involving this coenzyme [70, 71].

Later it was found that the determination of blood transaminase activities (AST and ALT) (more precisely their ratio, known as the de Ritis coefficient) could be used to diagnose liver and heart lesions [72].

Also, A.E. Braunstein and colleagues demonstrated that ammonia, released during the hydrolysis of the amide group of glutamine, was further incorporated into the ornithine cycle, where it was detoxified by converting into urea [73]. It has been indirectly shown that glutamine is a carrier of ammonia in the body. Its amount increased significantly due to the binding of ammonia at defects in the urea cycle.

Table 1. Diseases caused by collagen gene mutations. Adapted from [62]

Gene	Disease
COL1A1; *COL1A2*	Osteogenesis imperfecta (OI), osteoporosis
COL2A1	Chondrodysplasia, osteoarthrosis
COL4A3; *COL4A4*	Alport syndrome
COL5A1; *COL5A2*	Ehlers-Danlos syndrome (EDS) types I and II
COL9A1; *COL9A2*; *GOL9A3*	Multiple epiphyseal dysplasia, intervertebral disc disease, osteoarthrosis
COL1OA1	Metaphyseal chondrodysplasia, Schmid type
COL11A1; *COL11A2*	Non-Syndromic genetic hearing loss, osteoarthrosis
COL17A1	Generalized atrophic benign epidermolysis bullosa

A.E. Braunstein's pupil Vladimir Zinovievich Gorkin (later Corresponding Member of the Russian Academy of Medical Sciences) chose the study of the regulatory properties of monoamine oxidases (MAO), the most important enzymes of monoamine metabolism (serotonin, dopamine, tyramine, etc.), as the main focus of his scientific activity [74, 75]. Although by that time, the first MAO inhibitors had already been discovered and started to be used in clinical practice for the treatment of depressive disorders, they caused many side effects due to non-selective inhibition of the enzyme. In this context, one of the most important directions of V.Z. Gorkin's scientific activity included the search for molecules that would selectively inhibit MAO and thus reduce the number of unwanted effects [76–82].

Currently, MAO inhibitors continue to be used in the treatment of a wider range of psychiatric disorders: panic attacks, post-traumatic stress disorder, and neurodegenerative Parkinson's disease [83].

4. DRUGS/ANTIBIOTICS

Academician Mikhail Mikhailovich Shemyakin, whose name was given to the Institute of Bioorganic Chemistry, at the beginning of his career at IBMC headed a laboratory where the mechanisms of hydrolytic and oxidative-hydrolytic transformation of organic compounds were investigated [84–87]. The results of these studies helped to develop the theory of pyridoxal-dependent enzymes (in collaboration with A.E. Braunstein), to explain the mechanism of the Hooker reaction and the hydrolytic cleavage of some antibiotics [88]. In addition, M.M. Shemyakin investigated the structure, synthesis methods and mechanism of action of antibiotics. For example, the structures of auremicin and terramycin were determined [89] and some stages of synthesis of tetracyclines were described [90, 91]. The mechanism of action of levomycetin (chloromycetin) was investigated [92] and methods of its synthesis were developed [93, 94]. With minor modifications, these methods are still used in industry for the synthesis of this antibiotic.

5. GLUCOSE OXIDASE METHOD OF GLUCOSE DETERMINATION

Determination of glucose concentration is an important indicator for diagnostics and control of diabetes mellitus (type I, II, MODY, etc.), as well as gestational diabetes mellitus and steroid-induced diabetes. In 1960, Vladimir Konstantinovich Gorodetsky, an IBMC scientist, developed a method of blood glucose determination, which was a modification of the methods proposed by Middleton and Griffiths [95] and Marks [96]. This modification required a smaller amount of a sample used for one determination and a locally produced glucose oxidase preparation [97]. In addition, the method allowed selective determination of glucose in the presence of various sugars and other reducing non-carbohydrate substances. A little later, V.K. Gorodetsky and I.S. Lukomskaya produced a system of test strips for semi-quantitative determination of glucose in urine [98].

Modern methods of measuring glucose concentration work according to the same principles as the measurement methods of the past, but with minor modifications that contribute to increasing the sensitivity and stability of the methods.

CONCLUSIONS

This year IBMC celebrates its 80th anniversary. It should be emphasized that science in general and chemistry in particular is a field of human activity based on the experience and results accumulated by many generations of scientists and modern researchers should know and use these results for further developments in the field. Eight decades for IBMC is a history of successful activity, in which the contribution of each scientist was important. Biomedical chemistry is considered as the biological science of the XXI century. Predictive and preventive medicine, biosafety, operational measures in case of biological threats are modern challenges that form new vectors of development for the IBMC team.

REFERENCES

1. *Орехович В.Н.* (1933) К вопросу об активации протеолиза в регенерирующих тканях. Доклады Академии наук СССР, **1**(1), 118–122. [*Orekhovich V.N.* (1933) K voprosu ob aktivacii proteoliza v regeneriruyushchih tkanyah. Doklady Akademii Nauk SSSR, **1**(1), 118–122.]
2. *Reed C.E., Kita H.* (2004) The role of protease activation of inflammation in allergic respiratory diseases. J. Allergy Clin. Immunol., **114**(5), 997–1008. DOI: 10.1016/j.jaci.2004.07.060
3. *Vergnolle N.* (2016) Protease inhibition as new therapeutic strategy for GI diseases. Gut, **65**(7), 1215–1224. DOI: 10.1136/gutjnl-2015-309147
4. *Naveed M., Nadeem F., Mehmood T., Bilal M., Anwar Z., Amjad F.* (2021) Protease — A versatile and ecofriendly biocatalyst with multi-industrial applications: An updated review. Catal. Lett., **151**, 307–323. DOI: 10.1007/s10562-020-03316-7
5. *Razzaq A., Shamsi S., Ali A., Ali Q., Sajjad M., Malik A., Ashraf M.* (2019) Microbial proteases applications. Front. Bioeng. Biotechnol., **7**, 110. DOI: 10.3389/fbioe.2019.00110
6. *Казакова О.В., Орехович В.Н.* (1979) Катепсины D из нормальных органов и некоторых опухолей человека. Биохимия, **44**(10), 1762–1767. [*Kazakova O.V., Orekhovich V.N.* (1979) Cathepsins D from normal and neoplastic tissues. Biokhimiya, **44**(10), 1762–1767.]

7. *Логунов А.И., Орехович В.Н.* (1972) Выделение и свойства высокоочищенного катепсина А из селезенки быка. Биохимия, **37**(4), 855–861. [*Logunov A.I., Orekhovich V.N.* (1972) Isolation and some physico-chemical properties of purified cathepsin A from bovine spleen. Biokhimiya, **37**(4), 855–861.]
8. *Казакова О.В., Орехович В.Н.* (1963) Изучение свойств катепсинов I и II из перевиваемой крысиной саркомы М-1. Вопросы медицинской химии, **9**(5), 500–507. [*Kazakova O.V., Orekhovich V.N.* (1963) Izuchenie svojstv katepsinov I i II iz perevivaemoj krysinoj sarkomy M-1. Voprosy Meditsinskoi Khimii, **9**(5), 500–507.]
9. *Локшина Л.А., Лубкова О.Н., Гуреева Т.А., Орехович В.Н.* (1985) Изучение свойств и специфичности катепсина Н из селезенки быка. Вопросы медицинской химии, **31**(5), 125–130. [*Lokshina L.A., Lubkova O.N., Gureeva T.A., Orekhovich V.N.* (1985) Izuchenie svojstv i specifichnosti katepsina H iz selezenki byka. Voprosy Meditsinskoi Khimii, **31**(5), 125–130.]
10. *Логунов А.И., Орехович В.Н.* (1972) Субстратная специфичность катепсина А и его отношение к ингибиторам. Биохимия, **37**(5), 1061–1066. [*Logunov A.I., Orekhovich V.N.* (1972) Substrate specificity of cathepsin A and its attitude to inhibitors. Biokhimiya, **37**(5), 1061–1066.]
11. *Страчицкий К.И., Орехович К.Д.* (1949) О специфичности кристаллических протеиназ пищеварительного тракта. Вопросы медицинской химии, **1**(1–2), 151–158. [*Strachickij K.I., Orekhovich K.D.* (1949) O specifichnosti kristallicheskih proteinaz pishchevaritel'nogo trakta. Voprosy Meditsinskoi Khimii **1**(1–2), 151–158.]
12. *Орехович К.Д.* (1949) Сравнительная характеристика интенсивности ферментативного гидролиза различных белков кожи. Бюллетень экспериментальной биологии и медицины, **27**(1), 73–75. [*Orekhovich K.D.* (1949) Sravnitel'naya harakteristika intensivnosti fermentativnogo gidroliza razlichnyh belkov kozhi. Byulleten' Eksperimental'noy Biologii i Meditsiny, **27**(1), 73–75.]
13. *Орехович В.Н., Локшина Л.А., Троицкая О.В.* (1956) О концевых аминокислотах в пепсиногене. Доклады Академии наук СССР, **110**(6), 1041–1043. [*Orekhovich V.N., Lokshina L.A., Troickaya O.V.* (1956) O koncevyh aminokislotah v pepsinogene. Doklady Akademii Nauk SSSR, **110**(6), 1041–1043.]
14. *Локшина Л.А., Орехович В.Н.* (1957) Об активации пепсиногена. Биохимия, **22**(4), 699–701. [*Lokshina L.A., Orekhovich V.N.* (1957) On pepsinogen activation. Biokhimiya, **22**(4), 699–701.]
15. *Lokshina L.A., Orekhovich V.N., Sklyankina V.A.* (1964) Esterase activity of pepsin. Nature, **204**, 580. DOI: 10.1038/204580a0
16. *Локшина Л.А., Орехович В.Н.* (1966) Изучение действия ацетилимидазола на пепсин. Биохимия, **31**(1), 143–150. [*Lokshina L.A., Orekhovich V.N.* (1966) Investigation of the effect of acetylimidazole on pepsin. Biokhimiya , **31**(1), 143–150.]
17. *Розенфельд Е.Л., Попова И.А., Шубина А.И.* (1961) α-1,4-Экзополиглюкозидаза (γ-амилаза) печени. Биохимия, **26**(6), 1016–1021. [*Rosenfeld E.L., Popova I.A., Shubina A.I.* (1961) Liver α-1,4-exopolyglucosidase (γ-amylase). Biokhimiya, **26**(6), 1016–1021.]
18. *Михайлов В.П., Беленький Д.М., Розенфельд Е.Л.* (1978) Характеристика кислой α-глюкозидазы (γ-амилазы) печени человека как гликопротеин. Доклады Академии наук СССР, **242**(5), 1223–1225. [*Mihajlov V.P., Belen'kij D.M., Rozenfel'd E.L.* (1978) Harakteristika kisloj α-glyukozidazy (γ-amilazy) pecheni cheloveka kak glikoprotein. Doklady Akademii Nauk SSSR, **242**(5), 1223–1225.]
19. *Unnisa Z., Yoon J.K., Schindler J.W., Mason C., van Til N.P.* (2022) Gene therapy developments for Pompe disease. Biomedicines, **10**(2), 302. DOI: 10.3390/biomedicines10020302
20. *Rosenfeld E.L., Popova I.A., Chibisov I.V.* (1976) Some cases of type III glycogen storage disease. Clin. Chim. Acta, **67**(2), 123–130. DOI: 10.1016/0009-8981(76)90250-3
21. *Чибисов И.В., Карманский И.М., Шеляпина В.В., Леонтьев А.Ф., Розенфельд Е.Л.* (1978) Липопротеиды сыворотки крови при генерализованной форме гликогеноза III типа. Вопросы медицинской химии, **24**(4), 555–559. [*Chibisov I.V., Karmansky I.M., Shelyapina V.V., Leontiev A.F., Rozenfeld E.L.* (1978) Lipoproteins of blood serum in generalized form of glycogenosis type III. Voprosy Meditsinskoi Khimii, **24**(4), 555–559.]
22. *Rosenfeld E.L., Chibisov I.V., Karmansky I.M., Tabolin V.A., Chistova L.V., Leontiev A.F.* (1980) Serum lipoproteins of patients with glycogen storage disease. Clin. Chim. Acta, **102**(1), 99–104. DOI: 10.1016/0009-8981(80)90438-6.
23. *Еременко В.В., Евсеев Л.П., Николаев А.Ю.* (1968) Аспарагиназа *Bacterium cadaveris*. Микробиология, **37**(2), 207–212. [*Eremenko V.V., Evseev L.P., Nikolaev A.Y.* Asparaginase of *Bacterium cadaveris*. Mikrobiologiya, **37**(2), 207–212.]
24. *Мардашев С.Р., Еременко В.В., Николаев А.Я.* (1970) Идентификация *Pseudomonas sp.* и влияние условий выращивания на аспарагиназную и глутаминазную активности. Микробиология, **39**(1), 11–17. [*Mardashev S.R., Eremenko V.V., Nikolaev A.Ya.* (1970) Identification of *Pseudomonas sp.* and the effect of growth conditions on asparaginase and glutaminase activity. Mikrobiologiya, **39**(1), 11–17.]
25. *Pokrovskaya M.V., Pokrovsky V.S., Aleksandrova S.S., Sokolov N.N., Zhdanov D.D.* (2022) Molecular analysis of L-asparaginases for clarification of the mechanism of action and optimization of pharmacological functions. Pharmaceutics, **14**(3), 599–623. DOI: 10.3390/pharmaceutics14030599
26. *Sankaran H., Sengupta S., Purohit V., Kotagere A., Moulik N.R., Prasad M., Gota V.* (2020). A comparison of asparaginase activity in generic formulations of *E. coli* derived L-asparaginase: *In vitro* study and retrospective analysis of asparaginase monitoring in pediatric patients with leukemia. Br. J. Clin. Pharmacol., **86**(6), 1081–1088. DOI: 10.1111/bcp.14216
27. *Dobryakova N.V., Zhdanov D.D., Sokolov N.N., Aleksandrova S.S., Pokrovskaya M.V., Kudryashova E.V.* (2023) *Rhodospirillum rubrum* L-asparaginase conjugates with polyamines of improved biocatalytic properties as a new promising drug for the treatment of leukemia. Appl. Sci., **13**(5), 3373. DOI: 10.3390/app13053373
28. *Shishparenok A.N., Gladilina Y.A., Zhdanov D.D.* (2023) Engineering and expression strategies for optimization of L-asparaginase development and production. Int. J. Mol. Sci., **24**(20), 15220. DOI: 10.3390/ijms242015220
29. *Зыкова В.П., Пасхина Т.С.* (1965) Обнаружение калликреина в глобулиновой фракции белков сыворотки крови кролика. Доклады Академии наук СССР, **165**(6), 1439–1442. [*Zykova V.P., Paskhina T.S.* (1965) Obnaruzhenie kallikreina v globulinovoj frakcii belkov syvorotki krovi krolika. Doklady Akademii Nauk SSSR, **165**(6), 1439–1442.]

30. *Яровая Г.А., Доценко В.Л., Крижевская Ю.В., Морозова Н.А., Орехович В.Н.* (1979) Активирование прекалликреина сыворотки крови человека различными активаторами. Биохимия, **44**(7), 1279–1285. [*Yarovaya G.A., Dotsenko V.L., Krizhevskaya Yu.V., Morozova N.A., Orekhovich V.N.* (1979) Activation of prekallikrein from human blood serum. Biokhimiya, **44**(7), 1279–1285.]
31. *Егорова Т.П., Пасхина Т.С.* (1967) Очистка кининогена (брадикининогена) из плазмы крови кролика и изучение его свойств. Биохимия, **32**(2), 354–362. [*Egorova T.P., Paskhina T.S.* (1967) Purification of kininogen (bradikininogen) from rabbit blood plasma and study of its properties. Biokhimiya, **32**(2), 354–362.]
32. *Пасхина Т.С., Макевнина Л.Г., Егорова Т.П., Левина Г.О.* (1977) Идентификация кининов, освобождаемых панкреатическим калликреином свиньи из низкомолекулярного кининогена кролика. Биохимия, **42**(6), 1144–1147. [*Paskhina T.S., Makevnina L.G, Egorova T.P., Levina G.O.* (1977) Identification of kinins releasing by pig pancreatic kallikrein from rabbit low molecular weight kininogen. Biokhimiya, **42**(6), 1144–1147.]
33. *Бондарь З.А., Пасхина Т.С., Кринская А.В., Мелкумова И.С.* (1977) Значение определения уровня калликреиногена в крови при хронических заболеваниях печени. Советская медицина, **78**(2), 72–76. [*Bondar Z.A., Paskhina T.S., Krinskaya A.V., Melkumova I.S.* (1977) The importance of determining the blood kallikreinogen level in chronic affections of the liver. Sovetskaya Medicina, **78**(2), 72–76.]
34. *Пасхина Т.С., Полянцева А.Р., Егорова Т.П., Кринская А.В., Нартикова В.Ф.* (1979) Компоненты кининовой системы, свободные кинины и ингибиторы протеиназ в отечных жидкостях у больных с нефротическим синдромом. Вопросы медицинской химии, **25**(5), 588–599. [*Paskhina T.S., Poliantseva A.R., Egorova T.P., Krinskaia A.V., Nartikova V.F.* (1979) Kinin system components, free kinins and proteinase inhibitors in the edematous fluids of nephrotic syndrome patients. Voprosy Meditsinskoi Khimii, **25**(5), 588–599.]
35. *Баскова И.П., Пасхина Т.С., Полянцева Л.Р., Якубовская Р.И., Тиеро А.* (1983) Оценка с помощью хромоген субстратов показателей калликреин-кининовой и свертывающей систем в плазме крови больных с нефротическим синдромом. Вопросы медицинской химии, **29**(5), 96–99. [*Baskova I.P., Paskhina T.S., Polyantseva L.R., Yakubovskaya R.I., Tiero A.* (1983) Use of chromogenic substrates for estimation of components of kallikrein-kinin and blood coagulation systems in blood plasma of patients with nephrotic syndrome. Voprosy Meditsinskoi Khimii, **29**(5), 96–99.]
36. *Елисеева Ю.Е., Орехович В.Н.* (1963) Выделение и изучение специфичности карбоксикатепсина. Доклады Академии наук СССР, **153**(4), 954–956. [*Eliseeva Yu.E., Orekhovich V.N.* (1963) Vydelenie i izuchenie specifichnosti karboksikatepsina. Doklady Akademii Nauk SSSR, **153**(4), 954–956.]
37. *Елисеева И.Е., Орехович В.Н., Павлихина Л.В., Алексеенко Л.П.* (1970) Карбоксикатепсин — ключевой фермент двух систем, регулирующих кровяное давление. Вопросы медицинской химии, **16**(6), 646–649. [*Eliseeva I.E., Orekhovich V.N., Pavlihina L.V., Alekseenko L.P.* (1970) Karboksikatepsin – klyuchevoj ferment dvuh sistem, reguliruyushchih krovyanoe davlenie. Voprosy Meditsinskoi Khimii, **16**(6), 646–649.]
38. *Re R.N.* (2004) Mechanisms of disease: Local renin-angiotensin-aldosterone systems and the pathogenesis and treatment of cardiovascular disease. Nat. Clin. Pract. Cardiovasc. Med., **1**(1), 42–47. DOI: 10.1038/ncpcardio0012
39. *Bekassy Z., Lopatko Fagerström I., Bader M., Karpman D.* (2022) Crosstalk between the renin-angiotensin, complement and kallikrein-kinin systems in inflammation. Nat. Rev. Immunol., **22**(7), 411–428. DOI: 10.1038/s41577-021-00634-8
40. *Беркелиева С.Ч., Орехович В.Н., Малая Л.Т.* (1983) Изменение активности дипептидил-карбоксипептидазы при гипертонической болезни и её осложнениях. Кардиология, **11**, 71–76. [*Berkelieva S.Ch., Orekhovich V.N., Malaya L.T.* (1983) Changes in the activity of dipeptidyl carboxypeptidase related to essential in hypertension and its complications. Kardiologiya, **11**, 71–76.]
41. *Филатова М.П., Крит Н.А., Ковальчук О.В., Комарова О.М.* (1980) Синтез девятичленного пептидного ингибитора пептидилдипептидазы. Биоорганическая химия, **6**(11), 1605–1614. [*Filatova M.P., Krit N.A., Kovalchuk O.V., Komarova O.M.* (1980) Synthesis of a nine-membered peptide inhibitor of peptidyldipeptidase. Bioorganicheskaya Khimiya, **6**(11), 1605–1614.]
42. *Ларионова Н.И., Маслов Е.В., Елисеева Ю.Е., Павлихина Л.В.* (1982) Титрование активных центров ферментов обратимыми ингибиторами. Дипептидил-карбоксипептидаза — ингибитор SQ 20881 из яда змей *Bothrops jararaca*. Биохимия, **47**(8), 1332–1337. [*Larionova N.I., Maslov E.V., Eliseeva Yu.E., Pavlikhina L.V.* (1982) Titration of active sites of dipeptidyl-carboxypeptidase from bovine kidney cortex by the reversible inhibitor SQ 20881 from snake *Bothrops jararaca* venom. Biokhimiya, **47**(8), 1332–1337.]
43. *Федченко В.И., Веселовский А.В., Копылов А.Т., Медведев А.Е.* (2023) Поиск потенциальных гипотензивных пептидов в аминокислотной последовательности реналазы человека и их идентификация в протеолитических фрагментах этого белка. Биомедицинская химия, **69**(6), 403–408. [*Fedchenko V.I., Veselovsky A.V., Kopylov A.T., Medvedev A.E.* (2023) The search for potential hypotensive peptides in the amino acid sequence of human renalase and their identification in proteolytic fragments of this protein. Biomeditsinskaya Khimiya, **69**(6), 403–408.] DOI: 10.18097/PBMC20236906403
44. *Moreau M.E., Garbacki N., Molinaro G., Brown N.J., Marceau F., Adam A.* (2005) The kallikrein-kinin system: Current and future pharmacological targets. J. Pharmacol. Sci., **99**(1), 6–38. DOI: 10.1254/jphs.srj05001x
45. *Forrester S.J., Booz G.W., Sigmund C.D., Coffman T.M., Kawai T., Rizzo V., Eguchi S.* (2018) Angiotensin II signal transduction: an update on mechanisms of physiology and pathophysiology. Physiol. Rev., **98**(3), 1627–1738. DOI: 10.1152/physrev.00038.2017
46. *Yan R., Zhang Y., Li Y., Xia L., Guo Y., Zhou Q.* (2020) Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science, **367**(6485), 1444–1448. DOI: 10.1126/science.abb2762
47. *Noris M., Benigni A., Remuzzi G.* (2020) The case of complement activation in COVID-19 multiorgan impact. Kidney Int., **98**(2), 314–322. DOI: 10.1016/j.kint.2020.05.013
48. *Varga Z., Flammer A.J., Steiger P., Haberecker M., Andermatt R., Zinkernagel A.S., Moch H.* (2020) Endothelial cell infection and endotheliitis in COVID-19. Lancet, **395**(10234), 1417–1418. DOI: 10.1016/S0140-6736(20)30937-5

49. *Sibilla S., Godfrey M., Brewer S., Budh-Raja A., Genovese L.* (2015) An overview of the beneficial effects of hydrolysed collagen as a nutraceutical on skin properties: Scientific background and clinical studies. Open Nutraceuticals J., **8**(1), 29–42. DOI: 10.2174/1876396001508010029
50. *Shoulders M.D., Raines R.T.* (2009) Collagen structure and stability. Annu. Rev. Biochem., **78**(1), 929–958. DOI: 10.1146/annurev.biochem.77.032207.120833
51. *Wang H.* (2021) A review of the effects of collagen treatment in clinical studies. Polymers, **13**(22), 3868. DOI: 10.3390/polym13223868
52. *Орехович В.Н., Тустановский А.А., Орехович К.Д., Плотникова Н.Е.* (1948) О проколлагене кожи. Биохимия, **13**(1), 55–60. [*Orekhovich V.N., Tustanovskij A.A., Orekhovich K.D., Plotnikova N.E.* (1948) O prokollagene kozhi. Biokhimiya, **13**(1), 55–60.]
53. *Орехович К.Д.* (1950) О содержании проколлагена в коже животных различного возраста. Доклады Академии наук СССР, **71**(8), 521–522. [*Orekhovich K.D.* (1950) O soderzhanii prokollagena v kozhe zhivotnyh razlichnogo vozrasta. Doklady Akademii Nauk SSSR, **71**(8), 521–522.]
54. *Орехович В.Н., Павлихина Л.В.* (1957) О превращении проколлагена в коллаген. Вопросы медицинской химии, **3**(3), 195–201. [*Orekhovich V.N., Pavlikhina L.V.* (1957) The transformation of procollagen into collagen. Voprosy Meditsinskoi Khimii, **3**(3), 195–201.]
55. *Орехович В.Н., Тустановский А.А., Черников М.П.* (1949) Аминокислотный состав проколлагена. Бюллетень экспериментальной биологии и медицины, **11**, 372–374. [*Orekhovich V.N., Tustanovskij A.A., Chernikov M.P.* (1949) Aminokislotnyj sostav prokollagena. Byulleten' Eksperimental'noy Biologii i Meditsiny, **11**, 372–374.]
56. *Коган Г.Л., Берман А.Е., Мазуров В.И.* (1973) Биосинтез коллагена в бесклеточной системе в присутствии РНК, выделенных из полисом куриных эмбрионов. Биохимия, **38**(4), 872–874. [*Kogan G.L., Berman A.E., Mazurov V.I.* (1973) Biosynthesis of collagen in cell-free system in the presence of RNA isolated from the polysomes of the chicken embryos. Biokhimiya, **38**(4), 872–874.]
57. *Замараева Т.В., Инсарова И.Д., Мазуров В.И.* (1976) Биосинтез и свойства коллагена, образующегося в хрящевой ткани куриных эмбрионов в присутствии различных аналогов пролина. Вопросы медицинской химии, **22**(6), 830–834. [*Zamaraeva T.V., Insarova I.D., Mazurov V.I.* (1976) Biosynthesis and properties of collagen in cartilage of chick embryos in presence of various proline analogues. Voprosy Meditsinskoi Khimii, **22**(6), 830–834.]
58. *Оборотова Т.А., Берман А.Е., Мазуров В.И.* (1979) Биосинтез коллагена и других белков на прочно и непрочно связанных полирибосомах из куриных эмбрионов. Биохимия, **44**(9), 1715–1720. [*Oborotova T.A., Berman A.E., Mazurov V.I.* (1979) Biosynthesis of collagen and other proteins on tightly and loosely bound polyribosomes from chick embryos. Biokhimiya, **44**(9), 1715–1720.]
59. *Берман А.Е., Горнаева Н.П., Оборотова Т.А., Мазуров В.И.* (1980) Биосинтез коллагена в бесклеточной системе из зародышей пшеницы на поли(А)-РНК, выделенной из мембраносвязанных полирибосом куриных эмбрионов. Биохимия, **45**(1), 63–74. [*Berman A.E., Gornaeva N.P., Oborotova T.A., Mazurov V.I.* (1980) Biosynthesis of collagen in a cell-free system from wheat germs on poly(A)-RNA isolated from membrane-bound polyribosomes of chicken embryos. Biokhimiya, **45**(1), 63–74.]
60. *Златопольский А.Д., Белкин В.М., Зыкова Т.А., Мазуров В.И.* (1982) Взаимодействие ^{125}I-коллагена с растущими полипептидами фибронектина полирибосом куриных эмбрионов. Вопросы медицинской химии, **20**(2), 108–114. [*Zlatopolsky A.D., Belkin V.M., Zykova T.A., Mazurov V.I.* (1982) Interaction of ^{125}I-collagen with growing fibronectin polypeptides from chicken embryo polyribosomes. Voprosy Meditsinskoi Khimii, **20**(2), 108–114.]
61. *Орехович В.Н., Мазуров В.И.* (1960) Изучение α- и β-компонентов проколлагенов. Биохимия, **25**(5), 814–824. [*Orekhovich V.N., Mazurov V.I.* (1960) On α- and β-components of procollagen. Biokhimiya, **25**(5), 814–824.]
62. *Myllyharju J., Kivirikko K.I.* (2001) Collagens and collagen-related diseases. Ann. Med., **33**(1), 7–21. DOI: 10.3109/07853890109002055
63. *Wu G.* (2009) Amino acids: Metabolism, functions, and nutrition. Amino Acids, **37**(1), 1–17. DOI: 10.1007/s00726-009-0269-0
64. *Konikova A., Dobbert N., Braunstein A.* (1947) Labilization of the Î±-hydrogen of amino-acids in the presence of aminopherase. Nature, **159**, 67–68. DOI: 10.1038/159067a0
65. *Браунштейн А.Е., Горяченкова Е.В., Пасхина Т.С.* (1949) Энзиматическое образование аланина из L-кинуренина и L-триптофана и роль витамина В6 в этом процессе. Биохимия, **14**(2), 163–179. [*Braunshtejn A.E., Goryachenkova E.V., Paskhina T.S.* (1949) Enzimaticheskoe obrazovanie alanina iz L-kinurenina i L-triptofana i rol' vitamina B6 v etom processe. Biokhimiya, **14**(2), 163–179.]
66. *Браунштейн А.Е., Азарх Р.М.* (1950) Об участии витамина В6 в энзиматическом образовании сероводорода из L-цистеина. Доклады Академии наук СССР, **71**(1), 93–96. [*Braunshtejn A.E., Azarh R.M.* (1950) Ob uchastii vitamina B6 v enzimaticheskom obrazovanii serovodoroda iz L-cisteina. Doklady Akademii Nauk SSSR, **71**(1), 93–96.]
67. *Браунштейн А.Е., Горяченкова Е.В.* (1950) Участие витамина В6 в образовании цистеина путем энзиматического переноса серы. Доклады Академии наук СССР, **74**(3), 529–532. [*Braunshtejn A.E., Goryachenkova E.V.* (1950) Uchastie vitamina B6 v obrazovanii cisteina putem enzimaticheskogo perenosa sery. Doklady Akademii Nauk SSSR, **74**(3), 529–532.]
68. *Горяченкова Е.В., Азарх Р.М.* (1950) О роли витамина В6 в энзиматическом образовании таурина в печени. Вопросы медицинской химии, **2**, 224–230. [*Goryachenkova E.V., Azarh R.M.* (1950) O roli vitamina B6 v enzimaticheskom obrazovanii taurina v pecheni. Voprosy Meditsinskoi Khimii, **2**, 224–230.]
69. *Браунштейн А.Е., Виленкина Г.Ю.* (1949) Ферментативное образование глицина из серина, треонина и других гидроксиаминокислот в тканях животных. Доклады Академии наук СССР, **65**, 243–246. [*Braunshtejn A.E., Vilenkina G.Yu.* (1949) Fermentativnoe obrazovanie glitsina iz serina, treonina i drukih gidroksiaminokislot v tkanyah zhivotnyh. Doklady Akademii Nauk SSSR, **65**, 243–246.]
70. *Браунштейн А.Е., Шемякин М.М.* (1952) Теория процессов аминокислотного обмена, катализируемых пиридоксалевыми энзимами. Доклады Академии наук СССР, **85**(5), 1115–1118. [*Braunshtejn A.E., Shemyakin M.M.* (1952) Teoriya processov aminokislotnogo obmena, kataliziruemyh piridoksalevymi enzimami. Doklady Akademii Nauk SSSR, **85**(5), 1115–1118.]
71. *Браунштейн А.Е., Шемякин М.М.* (1953) Теория процессов аминокислотного обмена, катализируемых пиридоксалевыми энзимами. Биохимия, **18**(4), 393–411. [*Braunshtejn A.E., Shemyakin M.M.* (1953) Teoriya processov aminokislotnogo obmena, kataliziruemyh piridoksalevymi enzimami. Biokhimiya, **18**(4), 393–411.]

72. *Ewid M., Sherif H., Allihimy A.S., Alharbi S.A., Aldrewesh D.A., Alkuraydis S.A., Abazid R.* (2020) AST/ALT ratio predicts the functional severity of chronic heart failure with reduced left ventricular ejection fraction. BMC Res, Notes, **13**, 1–6. DOI: 10.1186/s13104-020-05031-3
73. *Северина И.С.* (1960) К вопросу о роли глютамина в процессе мочевинообразования. Биохимия, **25**(5), 847–854. [*Severina I.S.* (1960) On the role of glutamine in hepatic ureogenesis. Biokhimiya, **25**(5), 847–854.]
74. *Горкин В.З., Романова Л.А.* (1959) О некоторых свойствах моноаминоксидазы митохондрий печени и мозга крыс. Биохимия, **24**(5), 826–832. [*Gorkin V.Z., Romanova L.A.* (1959) Some properties of the mitochondrial monoamine oxidase of the rat liver and brain. Biokhimiya, **24**(5), 826–832.]
75. *Горкин В.З., Китросский Н.А., Кляшторин Л.Б., Комиссарова Н.В., Леонтьева Г.А., Пучков В.А.* (1964) О субстратной специфичности аминоксидаз. Биохимия, **29**(1), 88–96. [*Gorkin V.Z., Kitrossky N.A., Klyashtorin L.B., Komissarova N.V., Leontyeva G.A., Puchkov V.A.* (1964) On the substrate specificity of amine oxidases. Biokhimiya, **29**(1), 88–96.]
76. *Горкин В.З., Гриднева Л.И., Ермолаев К.М., Желязков Д.К.* (1963) Новый негидразинный ингибитор моноаминооксидазы. Доклады Академии наук СССР, **153**(2), 468–469. [*Gorkin V.Z., Gridneva L.I., Ermolaev K.M., Zhelyazkov D.K.* (1963) Novyj negidrazinnyj ingibitor monoaminooksidazy. Doklady Akademii Nauk SSSR, **153**(2), 468–469.]
77. *Веревкина И.В., Горкин В.З., Гриднева Л.И., Лерман М.И., Романова Л.А., Ходера А.* (1964) О торможении активности митохондриальных аминооксидаз некоторыми трициклическими соединениями. Доклады Академии наук СССР, **157**(1), 191–193. [*Verevkina I.V., Gorkin V.Z., Gridneva L.I., Lerman M.I., Romanova L.A., Hodera A.* (1964) O tormozhenii aktivnosti mitohondrial'nyh aminooksidaz nekotorymi triciklicheskimi soedineniyami. Doklady Akademii Nauk SSSR, **157**(1), 191–193.]
78. *Вина И., Горкин В.З., Гриднева Л.И., Кляшторин Л.Б.* (1966) О механизме торможения активности митохондриальных моноаминоксидаз паргилином. Биохимия, **31**(2), 282–290. [*Vina I., Gorkin V.Z., Gridneva L.I., Klyashtorin L.B.* (1966) On the mechanism of inhibitory effect of pargyline on enzymatic activity of mitochondrial monoamine oxidases. Biokhimiya, **31**(2), 282–290.]
79. *Ермолаев К.М., Гриднева Л.И., Майминд В.И., Горкин В.З.* (1967) Торможение активности моноаминооксидазы 2-N-ацетиламиноциклогексен-2-оном и родственными ему соединениями. Вопросы медицинской химии, **13**(3), 286–290. [*Ermolaev K.M., Gridneva L.I., Maimind V.I., Gorkin V.Z.* (1967) Inhibition of monoamine oxidase activity by 2-N-acetylaminocyclohexen-2-on and related compounds. Voprosy Meditsinskoi Khimii, **13**(3), 286–290.]
80. *Горкин В.З., Точилкин А.И., Андреева Н.И., Машковский М.Д., Журавлева Г.В., Колесникова М.А.* (1974) Исследование антимоноаминооксидазного действия и фармакологических свойств гидрохлорида 2,3-дигидро-1Н-бенз[d,e]изохинолина. Фармакология и токсикология, **37**(6), 651–655. [*Gorkin V.Z., Tochilkin A.I., Andreeva N.I., Mashkovsky M.D., Zhuravleva G.V., Kolesnikova M.A.* (1974) A research into the antimonoaminoxidase action and pharmacological properties of 2,3-dihydro-1H-benz/d,e/isoquinoline hydrochloride. Farmakologiya i Toksikologiya, **37**(6), 651–655.]
81. *Бауманис Э.А., Калниня И.Э., Москвитина Т.А., Козлов Л.В., Горкин В.З.* (1978) О множественности моноаминоксидаз: торможение изопропилгидразидом D,L-серина моноаминоксидазной активности митохондрий. Биохимия, **43**(8), 1496–1503. [*Baumanis E.A., Kalninya I.E., Moskvitina T.A., Kozlov L.V., Gorkin V.Z.* (1978) On the multiplicity of monoamine oxidases: Inhibition of mitochondrial monoamine oxidase activity by isopropylhydrazide of D,L-serine. Biokhimiya, **43**(8), 1496–1503.]
82. *Машковский М.Д., Горкин В.З., Аснина В.В., Веревкина И.В.* (1981) Влияние пиразидола и депренила на моноаминооксидазу кишечника крысы. Бюллетень экспериментальной биологии и медицины, **91**(3), 309–311. [*Mashkovsky M.D., Gorkin V.Z., Asnina V.V., Verevkina I.V.* (1981) Effect of pyrazidol and deprenyl on monoamine oxidase of the rat intestine. Byulleten' Eksperimental'noy Biologii i Meditsiny, **91**(3), 309–311.]
83. *Youdim M.B.H., Edmondson D., Tipton K.F.* (2006) The therapeutic potential of monoamine oxidase inhibitors. Nat. Rev. Neurosci., **7**(4), 295-309. DOI: 10.1038/nrn1883
84. *Шемякин М.М., Щукина Л.А.* (1948) Гидролитические и окислительно-гидролитические превращения хинонов. Журнал общей химии, **18**(11), 1925–1944. [*Shemyakin M.M., Shchukina L.A.* (1948) Gidroliticheskie i okislitel'no-gidroliticheskie prevrashcheniya hinonov. Zhurnal Obshchej Khimii, **18**(11), 1925–1944.]
85. *Швецов Ю.Б., Щукина Л.А., Шемякин М.М.* (1949) Гидролитические превращения окси- и ацетокситрикетонов тетрагидронафталинового ряда. Журнал общей химии, **19**(3), 498–506. [*Shvecov Yu.B., Shchukina L.A., Shemyakin M.M.* (1949) Gidroliticheskie prevrashcheniya oksi- i acetoksitriketonov tetragidronaftalinovogo ryada. Zhurnal Obshchej Khimii, **19**(3), 498–506.]
86. *Щукина Л.А., Хохлов А.С., Шемякин М.М.* (1951) Гидролитическое расщепление 3-окси-1,4-нафтохинона Журнал общей химии, **21**(6), 908–925. [*Shchukina L.A., Hohlov A.S., Shemyakin M.M.* (1951) Gidroliticheskoe rasshcheplenie 3-oksi-1,4-naftohinona. Zhurnal Obshchej Khimii, **21**(6), 908–925.]
87. *Шемякин М.М., Бочвар Д.А., Щукина Л.А.* (1952) О строении окисей непредельных соединений. Журнал общей химии, **22**(3), 439–442. [*Shemyakin M.M., Bochvar D.A., Shchukina L.A.* (1952) O stroenii okisej nepredel'nyh soedinenij. Zhurnal Obshchej Khimii, **22**(3), 439–442.]
88. *Шемякин М.М., Щукина Л.А.* (1957) Теория окислительно-гидролитических превращений органических молекул. Биохимия, **22**(1–2), 214–225. [*Shemyakin M.M., Shchukina L.A.* (1957) A theory of oxidative-hydrolytic transformations of organic molecules. Biokhimiya, **22**(1–2), 214–225.]
89. *Шемякин М.М., Щукина Л.А.* (1953) Строение ауреомицина и террамицина. Доклады Академии наук СССР, **89**(3), 499–500. [*Shemyakin M.M., Shchukina L.A.* (1953) Stroenie aureomicina i terramicina. Doklady Akademii Nauk SSSR, **89**(3), 499–500.]
90. *Шемякин М.М., Колосов М.Н., Арбузов Ю.А., Е Юй-Юань, Шен Хуай-юй, Склобовский К.А., Карапетян М.Г., Гуревич А.И.* (1959) Промежуточные стадии синтеза тетрациклинов. Доклады Академии наук СССР, **128**(1), 113–116. [*Shemyakin M.M., Kolosov M.N., Arbuzov Yu.A., E Yuj-Yuan', Shen Huaj-yuj, Sklobovskij K.A., Karapetyan M.G, Gurevich A.I.* (1959) Promezhutochnye stadii sinteza tetraciklinov. Doklady Akademii Nauk SSSR, **128**(1), 113–116.]

91. *Шемякин М.М., Колосов М.Н., Карапетян М.Г., Чаман Е.С.* (1957) Начальные стадии синтеза тетрациклинов. Доклады Академии наук СССР, **112**(4), 669–672. [*Shemyakin M.M., Kolosov M.N., Karapetyan M.G., Chaman E.S.* (1957) Nachal'nye stadii sinteza tetraciklinov. Doklady Akademii Nauk SSSR, **112**(4), 669–672.]
92. *Шемякин М.М., Колосов М.Н., Левитов М.М., Германова К.И., Карапетян М.Г., Швецов Ю.Б., Бамдас Э.М.* (1956) Зависимость антимикробной активности хлоромицетина от его строения и механизм действия хлоромицетина. Журнал общей химии, **26**(3), 773–782. [S*hemyakin M.M., Kolosov M.N., Levitov M.M., Germanova K.I., Karapetyan M.G., Shvecov Yu.B., Bamdas E.M.* (1956) Zavisimost' antimikrobnoj aktivnosti hloromicetina ot ego stroeniya i mekhanizm dejstviya hloromicetina. Zhurnal Obshchej Khimii, **26**(3), 773–782.]
93. *Шемякин М.М., Бамдас Э.М., Виноградова Е.И., Карапетян М.Г., Колосов М.Н., Хохлов А.С., Швецов Ю.Б., Щукина Л.А.* (1953) Изучение путей синтеза и синтез оптически-деятельных аналогов хлоромицетина (левомицетина). Журнал общей химии, **23**(2), 1854–1867. [*Shemyakin M.M., Bamdas E.M., Vinogradova E.I., Karapetyan M.G., Kolosov M.N., Hohlov A.S., Shvecov Yu.B., Shchukina L.A.* (1953) Izuchenie putej sinteza i sintez opticheski-deyatel'nyh analogov hloromicetina (levomicetina). Zhurnal Obshchej Khimii, **23**(2), 1854–1867.]
94. *Шемякин М.М., Бамдас Э.М., Виноградова Е.И., Витковский Д.П., Губерниев М.А., Орехович В.Н., Хохлов А.С., Швецов Ю.Б., Щукина Л.А.* (1954) Рацемизация L-трео-1-(*п*-нитрофенил-)-2-дихлорацетил-амино-1,3-пропандиола с последующим превращением рацемата в хлоромицетин (левомицетин). Журнал общей химии, **24**(11), 2076–2084. [*Shemyakin M.M., Bamdas E.M., Vinogradova E.I., Vitkovskij D.P., Guberniev M.A., Orekhovich V.N., Hohlov A.S., Shvecov Yu.B., Shchukina L.A.* (1954) Racemizaciya L-treo-1-(*p*-nitrofenil-)-2-dihloracetil-amino-1,3-propandiola s posleduyushchim prevrashcheniem racemata v hloromicetin (levomicetin). Zhurnal Obshchej Khimii, **24**(11), 2076–2084.]
95. *Middleton J.E., Griffiths W.J.* (1957) Rapid colorimetric micro-method for estimating glucose in blood and C. S. F. using glucose oxidase. Br. Med. J., **2**(5060), 1525–1527. DOI: 10.1136/bmj.2.5060.1525
96. *Marks V.* (1959) An improved glucose-oxidase method for determining blood, C.S.F. and urine glucose levels. Clin. Chim. Acta, **4**(3), 395–400. DOI: 10.1016/0009-8981(59)90110-x
97. *Городецкий В.К.* (1962) Энзиматический метод количественного определения глюкозы в крови с помощью отечественного препарата глюкозооксидазы, б.и., Каталог Российской Государственной Библиотеки (РГБ), Москва. [*Gorodetskii V.K.* (1962) Enzimaticheskij metod kolichestvennogo opredeleniya glyukozy v krovi s pomoshch'yu otechestvennogo preparata glyukozooksidazy, b.i., Katalog Rossijskoj Gosudarstvennoj Biblioteki (RGB), Moskva.]
98. *Городецкий В.К., Лукомская И.С.* (1965) Изготовление и применение тест-бумажек для экспресс-метода определения глюкозы в моче, Вопросы медицинской химии, **11**(5), 91–94. [*Gorodetskii V.K., Lukomskaia I.S.* (1965) Manufacture and use of test-paper for the express-method of glucose estimation in urine, Voprosy Meditsinskoi Khimii, **11**(5), 91–94.]

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ФОРМИРОВАНИЕ ОСНОВ БЕЛКОВОЙ ХИМИИ В ИБМХ

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80 лет назад был основан Институт биомедицинской химии (ИБМХ), который вначале назывался Институт биологической и медицинской химии Академии Медицинских Наук СССР. За первые десятилетия работы Института были проведены значимые исследования, которые не только способствовали более глубокому пониманию биохимических процессов в живом организме, но и заложили основу для дальнейшего развития этих областей.

Главные направления ИБМХ того времени касались структуры ферментов (в первую очередь различных протеаз), их субстратов и ингибиторов, роли ферментов углеводного обмена в развитии патологий, а также изучения механизмов гидролитического и окислительно-гидролитического превращения органических соединений, исследования белков соединительной ткани, в том числе коллагенов, изучения аминокислотного обмена.

Работы тех лет сложно найти в современных онлайн-базах литературных источников, поэтому данный обзор поможет понять ценность исследований, проведённых в ИБМХ за первые 40 лет работы, а также какое развитие получили данные направления в наше время.

Полный текст статьи на русском языке доступен на сайте журнала (http://pbmc.ibmc.msk.ru).

Ключевые слова: ферменты; химия белков

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