SCIENTIFIC AND TECHNICAL JUSTIFICATION OF CONCEPTUAL PROVISIONS OF PROTEOMICS OF DAIRY BUSINESS

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Abstract: The paradigm of formation of science about nitrogen-containing compounds (protein complex) of raw milk – Proteomics – is stated. The monitoring of fractional composition, possibility of extraction, modification and application of the whole protein complex, caseins and serum proteins, their fractions and derivatives allows to consider the traditional and innovative component of dairy business in an absolutely new light, based on nanoclusters and biotechnology. The road map of casein complex of raw milk is considered. The characteristic of the main fractions of casein, from the point of view of modern biotechnology of cheeses and cottage cheese is provided. The characteristic of serum proteins of raw milk in the native and denatured states and after the microparticulation directed into nanotubes is separately considered. The unimproved opportunities for the modernization of technologies of extraction of protein clusters with the receipt of products for import substitution with export orientation are emphasized. For the first time in the logistics of system analysis the problems of controlled proteolysis of albumins of milk – casein and serum proteins, with the receipt of products for clinical nutrition are considered.

Keywords: milk proteins, casein, whey proteins, amino acids, composition and properties of protein complex of milk, ways of receipt, ways of use

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INTRODUCTION. STATEMENT OF THE PROBLEM

According to [2] the postulates of LACTOOMICS offered [1] and adapted in print as the science about MILK, and to the principles of logistics of dairy business [3], it is advisable to put briefly some reasons down, in general, in respect of innovations and information technologies, about one of the main components of milk – PROTEINS (from Greek protey – the first) – a protein complex (nitrogen-containing compounds) as the anthem of life creation on our planet (according to F. Engels). In phenomenology logistics together with Glycoomics [4] and Lipidomics [5] the term Proteomics is used.

Proteins of milk (nitrogen-containing compounds) are present practically in all dairy products – there is no deproteinized milk (fat-free as opposed to fat and delactosylated as opposed to lactose) in nature (in practice) yet. “Pure” protein complex – milk protein concentrates, casein, its modification – caseinates and derivatives (hydrolyzates) – peptides, an amino acid pool; serum proteins as a whole and individually, and also their multiple derivatives are known in the industry in the form of industrial products. Traditional casein, except its designated purpose as food in dairy products, is known from joiner's glue to artificial caviar. I felt warm for long in a jumper of "casein wool" acquired as a memorable souvenir in Poland (1965) – the casein was Polish and the "wool" was Japanese. And all this set of irreplaceable food products, medical supplies and technical semi-finished products – proteins begins with the multicomponent composition of protein complex of raw milk, the aggregate data about the types and fractions of which, according to the information given by A. Tepel [6], with the modern interpretation by V. V. El'chaninov [7, 8, 9, 10], are stated below. At the same time, the postulates, known from biological chemistry and genetics, general in importance, composition, structure and the properties of native natural proteins do not naturally repeat, the emphasis is only on milk proteins which are part of the biosphere, in the light of Lactoomics.

OBJECTS AND METHODS OF STUDY

The total content (the initial stage of road map of raw milk) of albumins in milk is within the limits of 2.9 … 4.0% (the total content of nonprotein nitrogen is up to 0.035%), which should be considered within Proteomics in practice, especially when monitoring primary raw milk as a commercial product and when treating serum. This indicator determines, along with milk fat, the technology and economy of dairy business. Is completely determined by the level of

development of livestock production. The dairy industry correlates de facto with this indicator. Unfortunately, this indicator hasn't been formalized in this branch at the financial, technological and social levels in our country until recently. Table 1 provides the summary data on the content of albumins in a dry residual of raw milk [11].

It follows from the provided data that the protein component in raw milk is significant (at the level of 25.0%) in a solid and considerably differs by types, which naturally determines the status of received products – a complex, casein (without fractionation), whey proteins (generally, without fractionation). Table 2 provides the general characteristic about the content of protein fractions of raw (whole) milk.

The structures, main and minor components, genetic variations, polypeptide chain and amino acid pool of protein compounds of milk raw materials are diverse. They constantly replenish. The information of Professor K. K. Gorbatova [12] with additions by A. Tepel [6] is given below about the amino acid pool of main fractions of proteins of raw milk.

An exceeding information file of researches on the interpretation of primary structure of all fractions and genetic variations with the elements of poetic allegory and a practical component is at the back of each digit. For example, the polypeptide chain can give a sweet (aspartame) and a bitter taste in cheeses; it is possible to receive antibiotics (nisin) and, unfortunately, poison. And this all can be received from the protein structure of milk.

The elementary composition of milk proteins (for your reference) according to various researchers [6, 12] is accurately traced in a hierarchy, with the contents at the level of, %: carbon (C) – 53.0, oxygen (O) – 23.0, nitrogen (N) – 15.6, hydrogen (H) – 7.0, sulfur (S) – 1.5, phosphorus (P) – 0.8.

Table 1. Content of albumins in raw milk

Description of raw material	Content of		%
	Solids, g/100ml	Protein, g/100ml	
Raw milk	13.30	3.20	24.06
Cream, fat percentage 35%	41.30	2.40	5.81
Non-fat milk, fat percentage 0.05%	8.70	3.20	36.80
Butter milk	9.10	3.20	35.16
Whey	6.30	0.80	12.70

Table 2. Main groups of albumins of raw milk

Name of fractions	Content, g/100ml	%
Total content	3.27	100.0
Total of caseins	2.60	79.5
including:		
α_{S1}-casein	1.00	30.6
α_{S2}-casein	0.26	8.0
β-casein	10.01	30.8
k-casein	3.30	10.1
Total of serum proteins	0.63	19.3
including:		
α-lactalbumin	0.12	3.7
β-lactoglobulin	0.32	9.9
blood serum albumin	0.04	1.2
immunoglobulins	0.07	2.1
proteosopeptones	0.08	2.4
proteins of fat globules membranes	0.04	1.2
minor proteins	trace amounts	–

Table 3. Amino acid pool of main fractions of proteins of raw milk

Fractions of polypeptide chain	Amino acid pool, pcs.·α-AA
α_{S1}-casein	199
α_{S2}-casein	207
β-casein	209
k-casein	169
α-lactalbumin	123
β-lactoglobulin	162
blood serum albumin	582

The content of the main component of nitrogen-containing compounds of milk – casein is up to 80% of protein complex and is 2.6 … 3.2% (the more the better). Casein has a lot of fractions (it is considered that there are more than 20 now), genetic variations, fragments and groups (from 1 to 6 for each fraction), which is little considered in practice yet, for example, in cheese making and in the production of cottage cheese. A purposeful search with the use of all achievements of modern analytics of organic compounds is necessary.

The content of whey proteins – at the level of 20% (not to confuse with whey proteins) in milk is 0.4 … 0.7%. Whey proteins of milk, just as casein, are fractional – up to 19 names with 7 genetic variations. The same goes to proteins o covers of fat globules (8 fractions). It is necessary within Lacoomics to point to a special, quite a new group of nitrogen-containing compounds, – minor (a low content, an important role) proteins – up to 2% of total mass (9 fractions and the mass of genetic variations).

In general, macrocomponents (casein and whey proteins) and the minor component allow to draw a conclusion about a genetically full-weight set of clusters of nitrogen-containing compounds in milk, an irreplaceable food component during all the life cycle of mammals. From exactly this perspective, in relation to industrial processing of raw milk, this group of compounds shall be considered for all the assortment groups of products and production cycles. It is not really available in the existing study books yet!

The methodology of study of albumins of raw milk and the received products is quite enough fulfilled [13, 14]. Is based on the gnoseology of coefficient 6.38 for nitrogen and the indispensability of Kyeldal's formula. At the same time, "the floating indicator of self-deception" for nonprotein nitrogen (NPN) in milk reaches 8%, and 30% in whey. Devices like MilkoScan neutralize this problem, but they are not absolutely recognized. There are breakthroughs, especially in the field of chromatography – gas, liquid and ionic chromatography [15]. For dairy business, of special interest are HPLC with reversed phases (RP-HPLC), fast protein liquid chromatography (FPLC) and size-exclusion chromatography (SEC), and also gel filtration, applicable for casein and serum proteins.

RESULTS AND DISCUSSION

Modern classification and nomenclature of milk proteins (is constantly replenishing and changing) [6, 12]. It is necessary to emphasize within Lactoomics and Proteomics the earlier mentioned polycomponent character of all four groups of milk proteins (caseins, whey proteins, protein of fat globules membranes, minor proteins) and to reconcile it once again with the road map of practical use of components, as a whole. Separately – with a possibility of modification for the primary components – peptides and amino acids, and also microparticulation. In such a logic of knowledge and analysis the modern postulates of Proteomics are considered. They are in the dynamics of development according to the achievements of fundamental sciences and practice of researches of creative teams of the international "dairy community".

Let us consider the road map, in respect of technological monitoring, of each of the macrocomponents of milk protein complex. At the same time, we use the information file obtained from survey information [16] and an education guide [17], special researches [18, 19, 20], system publications [7–10] and the generalizing material [6].

Caseins, from the perspective of Lactoomics and Proteomics, are of special cognitive and practical interest. They draw attention of theorists and practitioners as ideal natural protein (especially in respect of polymorphism) and a source of profit for business since the time of a curious Dutch practician Mulder and the great scientist Gammersten. The depth of cognition of milk casein and the constant attention to this problematics is confirmed by the information stated above, and also by my personal observations at special IDF World Dairy Summits in the Netherlands (1973) and Austria (1975). This subject is discussed in all the events of IDF and at all Industry Summits. And the need of interest for the object of cognition can be confirmed with a simple question, which is not cleared up yet, – "why is milk white?". The trick is in casein. The confirmation follows from an observation, trivial and available to everyone, of color of milk after spontaneous or controlled (heating – cooling – souring) souring – serum is transparent with a yellowish-greenish shade, and the product is of white color.

Fig. 1 provides the modern model of casein in the system HyperChem using the example of k-casein. It is considered that it reminds figuratively a jumping horse – there is nothing to do for chemists, physicists and biotechnologists but to "bridle a racer".

Even more indicative is the computer model of casein clusters on the basis of fractal views. Fig. 2 provides the systematized information by Smykov [19] about the models of aggregation of clusters of casein micelles: diffusion limited aggregation (DLA) [21]; ballistic aggregation (BLA) [22–24]; rotation limited aggregation (RLA) [25–28]; diffusion limited cluster aggregation (DLCA) [29]; reaction limited cluster aggregation (RLCA) [30–32]; ballistic limited cluster-cluster aggregation (BLCA) [33–36].

The provided compositions of clusters characterize the alternative variants of process of structurization ("clotting") of casein micelles (daily performed by cheesemakers). They also cover the allegory of "the synthesis of the Universe" in case of the thermal denaturation of serum proteins (try it by holding your own observation). These provisions are interpreted by the outstanding author of the term and theory of fractals, American academician Benoit Mandelbrot [37], they underline the uniqueness of casein as an object of biocenosis in the Universe. And confirm once again the whey phenomenon.

The genetic polymorphism of casein is well seen in the chromatogram (Fig. 3).

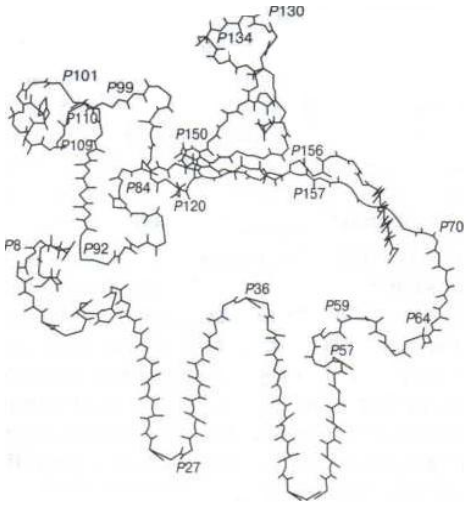


Fig. 1. Variant of visualization of model of micelle of k-casein according to HyperChem – public information.

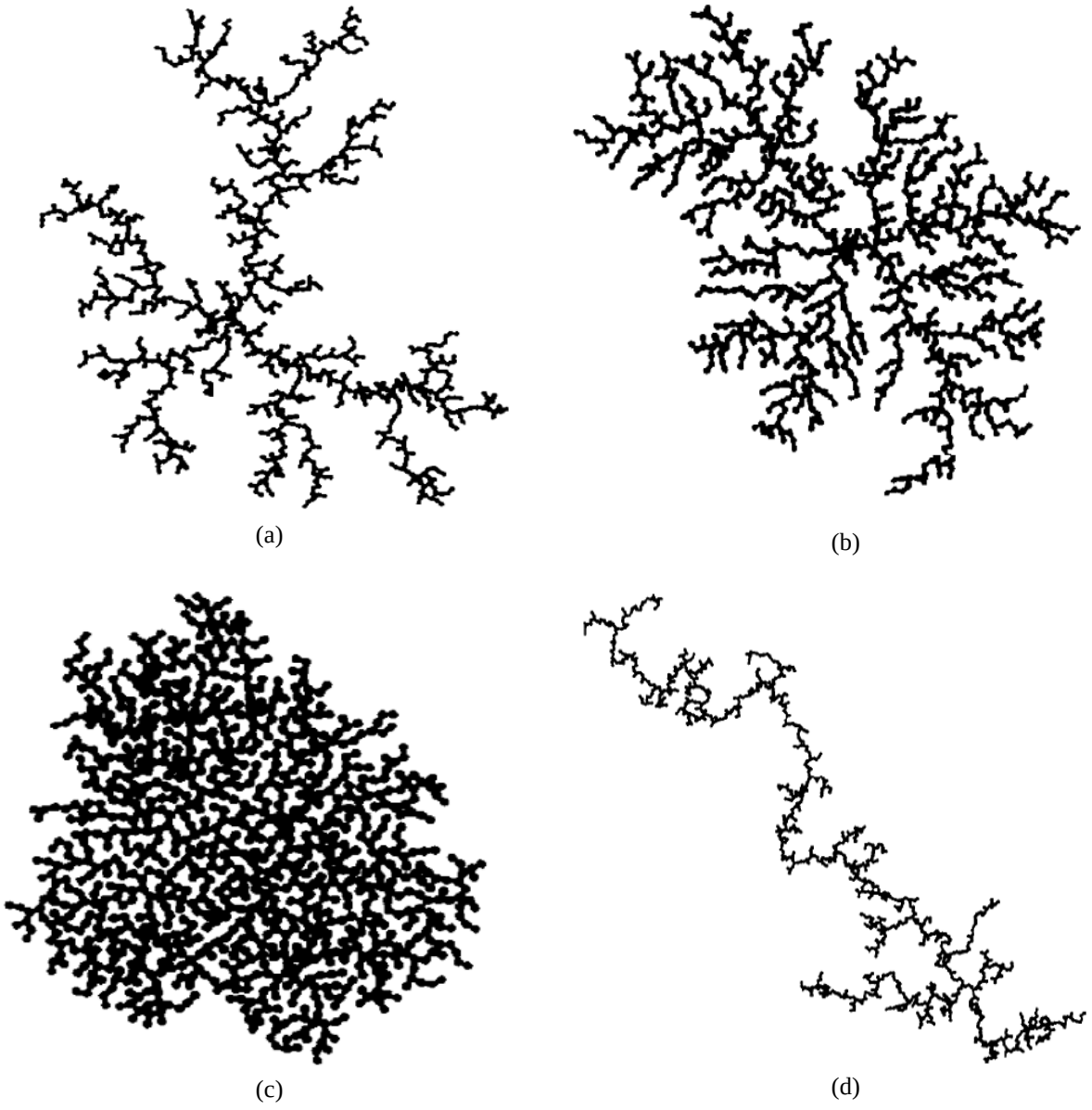
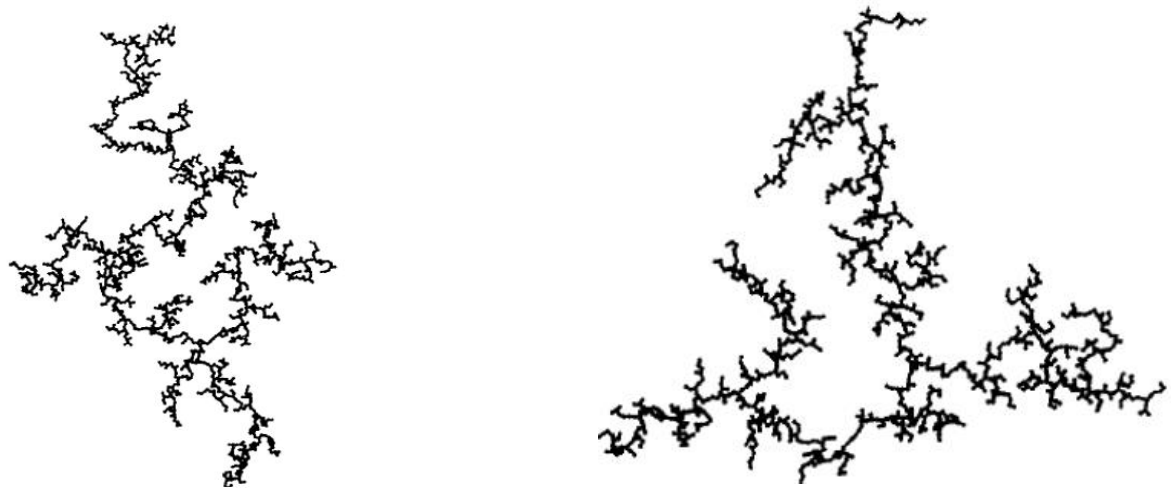


Fig. 2. *Beginning*. Computer models of formation of casein clusters: (a) DLA, (b) BLA, (c) RLA, (d) DLCA, (e) RLCA, and (f) BLCA.



(e) (f)

Fig. 2. *Ending*. Computer models of formation of casein clusters: (a) DLA, (b) BLA, (c) RLA, (d) DLCA, (e) RLCA, and (f) BLCA.

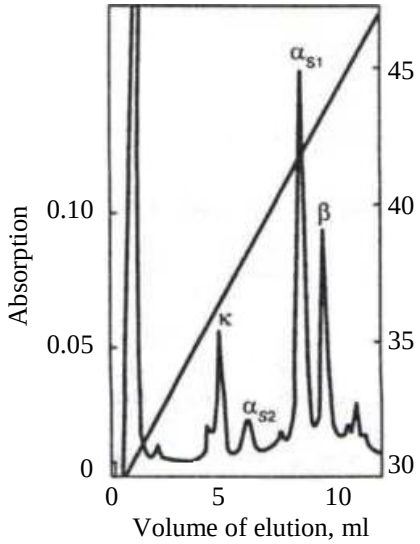


Fig. 3. Chromatogram of milk caseins.

The primary structure of casein, – a consecutive compound of amino acids, depends on a type of fraction and its genetic variation. This fine picture, worthy of "poetization", should be the cornerstone of Proteomics and demands individual consideration. The controlled hydrolysis (proteolysis) of protein compounds of casein and serum proteins turns into an independent branch which should be mastered in the dairy industry (the meat industry has earlier given complete control over it) – there were special shops by meat-processing plants. Are considered separately in respect of the controlled phenylalanine elimination.

The secondary structure – peptides, is already in technology [38] and will be considered below.

The tertiary structure of proteins is of great importance for the technological properties of milk. The three-dimensional tertiary structures can only be established in the previously crystallized proteins during the research by means of the X-ray diffraction analysis. It was not possible to perform casein crystallization till now – it is considered that it is hardly possible [6]. Is it the second problem for cognition, for example, in Skolkovo or within IDF?! The associates of micelles form a number of variants of quarternary structure of casein which is unstable and constantly demands the controlled regulation by processing methods (temperature, active acidity, mechanical effect).

95% of casein in its native state is in the type of casein micelles or associations of subunits (casein submicelles) which are the complexes of casein monomeric molecules. The behavior of milk during technological processing and industrial conversion is determined generally by the properties of casein micelles. The size of casein micelles is from 30 (nanolevel) to 300 (colloidal state), they have a spherical shape. It is they what determines the so-called yield of protein and fat products – cottage cheese and casein.

Whey proteins are polymorphic, which is well seen in the chromatogram (Fig. 4), their structure is unique (Table 4) and their rheomorphism is incomparable (Fig. 5). Their nanosize – at the level of 10 nanometers – is accurate, which forms, along with lactose, an authentically soluble system of milk (serum and ultrafiltrates). The protein complex of whey is specific, for example, due to the availability of k-casein, and demands individual consideration with the elements of repetition with Table 2.

Lactoglobulin (β-LG) – the main whey protein is non-uniform in structure. It is presented by several genetic variations A, B, C, D, E, F and G differing in amino acid structure. Their content is 50–60% of the total of serum proteins.

Lactoalbumin (α-La) is the second protein in order of importance, it is presented by the genetic variations A and B.

Immunoglobulins (IgG) is a non-uniform group of proteins – glycoproteids of monomers and polymers IgG1, IgG2, IgA and IgM.

Serum albumin (Sa) is presented by a polypeptide chain folded in four bound disulfide threads of globular segments of non-uniform proteins.

Lactoferrin, as well as transferrin, is an iron blood protein.

Osteopontin (OPN) – a multifunctional protein, is found recently, plays an important role in preserving the immune status of the newborns.

All fractions of whey proteins have small sizes and high hydrophily, which explains their high stability in solution. Unlike casein, whey proteins do not form micelles, do not coagulate under the effect of enzymes and do not precipitate in case of milk souring. A thermal effect (denaturation) is required for the realization of this process. Whey proteins have a rather low molecular weight – from 14 000 to 69 000.

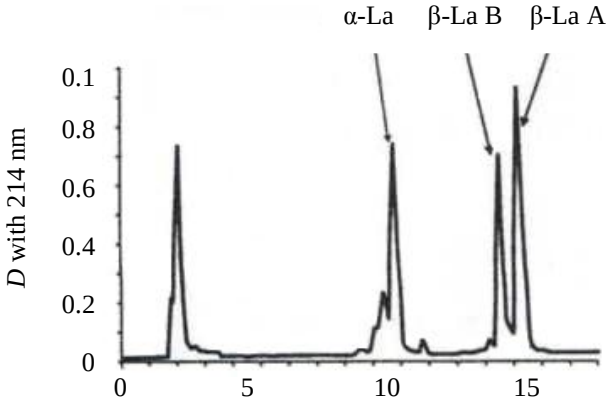
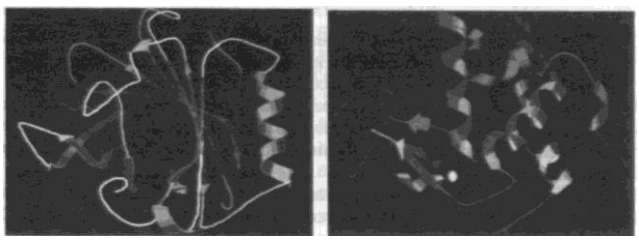


Fig. 4. Chromatogram of whey proteins.

Table 4. Characteristic of milk serum proteins

Name of fractions	Content, %	Molal weight
β-lactoglobulin	0.32	18 400
α-lactalbumin	0.12	14 000
Proteose-peptone fraction	0.12	from 10 000 to 200 000
Immunoglobulins	0.09	160 000
Serum albumin	0.03	70 000
Lactoferrin	0.02	93 000
L-Carnitine	0.03	–
Osteopontin	trace amounts	–
Total	0.73	–



β-lactoglobulinα-lactalbumin

Fig. 5. Molecular structures of some whey proteins.

Minor proteins of milk and **protein compounds of fat globules membranes** draw an increasing attention which obviously follows from the materials of seven International Whey Conferences, especially that of the fifth and sixth ones [39, 40]. For example, angiogenin was the subject of special researches [41] but the result is an original drug Milkang [42], which waits for its practical realization.

The derivation (receipt) of proteins from raw milk is an indispensable component of Proteomics and is constantly studied in respect of scientific knowledge for practical application [43].

The receipt of a **complex of milk proteins** in the form of milk protein concentrates is developed and relates to the basic researches [6, 16]. Unfortunately, this attractive technology is not widely scaled because of an inevitable loss of native properties. The problem waits for a decision. Our researches on soft cheeses [44, 45], cottage cheese products [46], the formation of the brand "LipKA" (a lipid casein albumin concentrate) [47] and the method "TermoLakt" [48], with an attempt to implement the paradigm of complex release of proteins from raw milk, confirm this provision. A search of the optimal solution within Proteomics is forthcoming. Probably, in this case the breakthrough innovations of Professor Z.S. Zobkova and her colleagues concerning enzymatic cross-linking of milk proteins are quite perspective, for example, using transglutaminase for the receipt of new structures and original functions of the derived special purpose products [49].

Coagulation of raw milk caseins – acid, rennet, acid and rennet, chlorcalcic coagulation, coagulation with the use of electrophysical methods, polysaccharides and membrane technology is quite well studied by and is applied at the level of traditions and innovations [11]. The traditions are acid and rennet coagulations. The innovations are membrane technologies (ultrafiltration). The supertechnologies are the biomembrane technology with the use of polysaccharides (membraneless reverse osmosis) and microparticulation (nanotubes).

The whey protein complex, in respect of release, is quite well studied and realized in practice [10]. The traditions are thermal denaturation; the innovations are membrane technologies. The supertechnologies are microparticulation (nanotubes).

The fundamentals of development of technology of dairy products, using the example of casein coagulation – (Laktoomics base), were worked out by A.M. Osintsev [18] in a system type. The complex extraction of milk proteins using the example of soft cheeses is thoroughly studied by I.A. Smirnova [50] and O.A. Suyunchev [48]. They are widely realized (scaled) in practice. However, the search is not finished. As an example, we will briefly consider "the membraneless technology", one of the alternative variants of extraction of casein with the implementation in the line (series) of products of the brand "Bio-TON" [51].

Historically, the cycle of development of new technology of thermodynamic fractionation of milk components (sometimes called as membraneless reverse osmosis) includes the stage of accidental observations in the thirties of spontaneous milk separation when adding polysaccharide (Patent DE 555273) for two fractions – casein concentrate and a serum fraction. It was the stage which proved a unique possibility of separation of milk into a casein and non-casein fractions. The method did not find practical application and was forgotten for more than 50 years. Then, at A.N. Nesmeyanov Institute of Organoelement Compounds (INEOS) of Academy of Sciences of the USSR, within a number of large-scale basic researches of Professor V.B. Tolstoguzov and his colleagues studying the problem of search of food reserves, a possibility of controlled separation of protein solutions by polysaccharides was theoretically proved and experimentally demonstrated. Milk was one of the ideal objects. In the State Enterprise «Scientific Research Institute of the Complex Utilization of Dairy Raw Material (formerly known as All-Union Research Institute of the Complex Utilization of Dairy Raw Material and The North Caucasian branch of All-Union Research Institute of the Cheesemaking and Buttermaking Industry) by efforts of the school of my dear colleague from RAS Professor V.V. Molochnikov complex specific researches [52, 53] on the development of non-waste technology of fractionation of milk by polysaccharides using the principle of membraneless return osmosis [54], which was named as "Bio-Ton", were performed.

Fig. 6 provides the schematic diagram of separation of milk by biopolymers (polysaccharides).

As a result of separation, natural casein concentrate is received, the characteristic of which (in respect of Proteomics) we will consider in more detail [55].

Natural casein concentrate (NCC) is a light-cream thixotropic uniform liquid with creamy consistence and with a pure milk taste and smell. It completely dissolves in water. The thermal effect up to 100°C on liquid natural casein concentrate does not change its solubility, which testifies to naturalness as it is known that milk casein has a unique structure in its native state, which specifies its resistance to the effect of denaturant agents and its high splittability by proteolytic enzymes.

Table 5 provides the average physical and chemical values of NCC in comparison with skim milk.

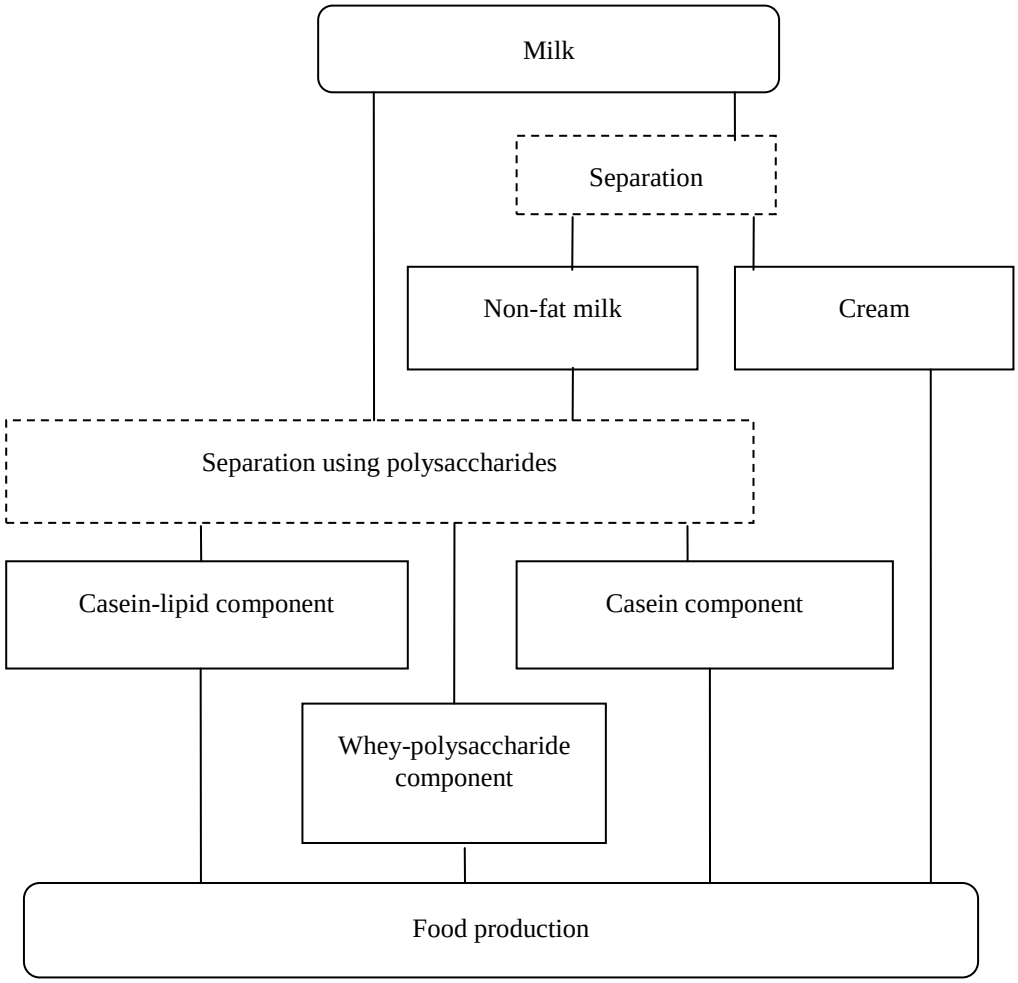


Fig. 6. Schematic diagram of separation of milk by polysaccharides.

Table 5. Average physical and chemical values of NCC in comparison with non-fat milk

Parameters	Skim milk	NCC	Ratio, %
Percentage of solids, % including: protein, %	 8.70 ± 0.20 3.15 ± 0.15	 19.45 ± 0.50 13.75 ± 0.50	 223.6 436.51
lactose, %	4.75 ± 0.05	3.60 ± 0.10	75.8
pectin, %	–	–	0.70% in the mix of FTIR
minerals, %	0.75 ± 0.05	1.80 ± 0.10	240
fat, %	0.05 ± 0.00	0.25 ± 0.05	500
Calcium, mg/100g	115 ± 5	400 ± 10	347.8
Phosphorus, mg / 100 g	95 ± 5	250 ± 10	263.2
Titrable acidity, ^{o}T	18 ± 2	50 ± 2	278
Active acidity, pH	6.7 ± 0.1	6.3 ± 0.2	< 0.40
Density, kg/m^3	1030 ± 5	1060 ± 15	> by 30

Natural casein concentrate contains the main components – proteins, carbohydrates, minerals in a soluble form. The main protein component of NCC is casein in the form of casein-calcium-phosphate complex, which allows to keep, to a wide extent, the natural properties of the main milk protein. The considerable part of calcium and phosphorus transits into NCC, which provides the preservation of mineral balance in the derived milk casein complex. The fractional composition of natural casein concentrate, in respect of electrophoretic mobility, completely coincides with the samples received in the traditional acid way. The residual fat of milk is taken away by the protein part and is concentrated in it in the course of release of casein. The high values of titrable acidity in natural casein concentrate are caused by the presence of concentrated protein and mineral salts. The increase in the percentage of proteins, carbohydrates and minerals in the concentrate increase its density up to 1060–1070 kg/m^3 in comparison with skim milk. The presence of minerals, a quantity of lactose and milk fat concentrated together with the casein-calcium-

phosphate complex of milk increases the nutrition value of products in the course of its use [56].

The main protein in NCC is casein, its content is about 98%, the content of whey proteins is insignificant and does not exceed 3%. Skim milk is separated as follows during fractionation: up to 85% of volume is a whey-polysaccharide fraction, and 15% is a casein fraction which contains about 20% of solids, including about 14% of protein. Thus, casein concentrate contains up to 70% of protein, and 30% are the components of whey-polysaccharide fraction (WPF). With such a ratio the casein complex preserves its native properties, without changing them even after drying.

"The life cycle" of Proteomics of NCC just begins.

Of special interest within Proteomics of dairy business is the receipt of **derivatives of protein complex of milk** – casein and whey proteins. This subject deserves special consideration. At the same time, separation using hydrolysis and proteolysis must be kept in mind. Casein hydrolysis is not only studied, but is also realized in practice throughout the world, including our country, for example, in drugs. Casein proteolysis in cheese – the basis of its biotechnology, determines the type and quality of a product. The hydrolysis of whey proteins has a special value in the medical-biological aspect – for baby, dietary and clinical nutrition. Let us show the significance of object, complexity of process and uniqueness of result using the example of the large-scale researches of the creative team of Professor A.Yu. Prosekov (Kemerovo Institute of Food Science and Technology) and, in particular, the works by O.O. Babich [20].

The biologically active peptides received from milk proteins are realized in the industrial technologies of developments of Kemerovo Institute of Food Science and Technology in England (according to the existing international rules). This alone, in respect of the Proteomics of dairy business, draws attention, does credit to the developers and confirms the opportunity of realization of not only import substitution of products, but also of export of innovative technologies. The informative part of researches and the obtained results are published in a special monograph [38]. Let us only consider the innovative priorities for the confirmation of postulates of Proteomics using a specific example. It is necessary to pay attention to a special role of natural polypeptide chains of amino acids (contained in raw milk) and those which are purposefully synthesized from fractions of casein and serum proteins (from tens to hundreds). For example, exomorphins are analgetics. They regulate the general hormonal background of mammals, especially that of cubs (there is no crying). And beta-casomorphins are fine immunomodulators. "Dairy peptides" increase the phagocytic ability of some bacteria of GIT, providing the resistance of the organism to infectious diseases. For example, the analog of low-molecular peptide of women's milk – lactoptin, synthesized recently in Institute of Chemical Biology and Fundamental Medicine, Siberian Branch of the Russian Academy of Sciences, has an antineoplastic and anti-metastatic activity and is absolutely safe. Angiogenin Milkang [42] plays the same role, in respect of blood vessels, wounds and burns.

Taking into account the above stated, predicting the results of exploratory researches given below, the formation of an independent section of Laktoomics with the brand of Peptidomics of dairy business is absolutely appropriate!

Table 6 provides the efficiency of hydrolysis of the basic casein fractions using various enzymatic drugs.

The analysis of the data provided in Table 6 shows that the nature of change of nitrogen of casein fractions by all the enzymes is approximately identical. Trypsin effectively hydrolyzes a k-fraction, providing a decrease in the content of nitrogen by 16.9%. Chymotrypsin and thermolysine transform the transition of some fractions of casein to other forms of nitrogen compounds. The identification of the received sequences of peptides according to the database NCBI [38] is given in Table 7.

The results of identification clearly show that the fermentation by all the tested drugs – trypsin, chymotrypsin and thermolysine provide the receipt of biologically active peptides. Table 8 specifies the optimum parameters of average and high extent of hydrolysis of casein fractions for receiving biologically active peptides with their crucial indicators.

Table 6. Total content of albumins in hydrolyzates

Sample	Percentage of nitrogen of casein fractions, mg/100g			
	α	β	γ	χ
Before fermentation	0.202	0.083	0.019	0.071
After fermentation by trypsin	0.196	0.073	0.017	0.045
After fermentation by chymotrypsin	0.195	0.080	0.018	0.055
After fermentation by thermolysin	0.198	0.081	0.018	0.064

Table 7. Peptides identified in the studied hydrolyzates

Fragment	Used enzyme	Sequence of amino acids in peptides	Name	Function
1–25	Trypsin, chymotrypsin	Arg-Glu-Leu-Glu-Glu-Leu-Asn-Val-Pro-Gly-Glu-Ile-Val-Glu-Ser(P)-Leu-Ser(P)Ser(P)-Ser(P)-Glu-Glu-Ser-Ile-Thr-Arg	phosphopeptide	stimulation of digestion of mineral substances
177–183	thermolysin	Aia-Val-Pro-Tyr-Pro-Gln-Arg	P-kasokinin	the inhibitor of angiotensin converting enzyme

Table 8. Technological characteristics of the process of enzymatic hydrolysis

Parameters of process and characteristic of hydrolyzates	Casein after treatment with		
	trypsin	chymotrypsin	thermolysin
Solids in solution, %	5.18	4.98	4.80
Quantity of enzyme of the weight of substratum, %	0.01	0.01	0.01
Temperature of process, °C	50 ± 1		
pH of process	7.4÷7.6	7.4÷7.6	7.4÷7.6
Process duration, hrs	12	12	10
Temperature of enzyme inactivation, °C	93 ± 2		
Inactivation duration, min	5		
Molar weight, kD	4.5	3.1	3.1

Anti-gene activity (AG) as an objective criterion of biological safety of the received peptide drugs, in relation to pasteurized milk, is shown below.

Sample	AG (in relation to whole pasteurized cow milk)
Casein	0.79
Filtrate of tryptic hydrolyzate through a membrane of 10 kD	$7.5*10^{-6}$
Filtrate of chymotryptic hydrolyzate through a membrane of 10 kD	$3.7*10^{-6}$
Filtrate of thermolysin hydrolyzate through a membrane of 10 kD	$5.8*10^{-6}$

The given indicators of the decrease in AG in all the hydrolyzed samples, one million times in comparison with the initial substratum (milk protein) – are comparable to the characteristic of the specialized mixes proved by practice, for example, "Nutramigen" and other mixes.

In general, the purposeful researches on the currently important problematic performed by O.O. Babich, allowed to determine the main regularities of the process of hydrolysis of milk proteins with the receipt of biologically active peptides for specialized foodstuffs. Based on the same scientific paradigm, O.O. Babich performed a number of system researches [20] on the receipt of casein hydrolyzates and serum proteins with a regulated amino-acid pool, which also forms a portfolio of innovations of Laktoomics using the example of development of Proteomics, after Peptidomics.

The amino-acid pool of proteins of raw milk, with its uniqueness, can serve as an ideal for food of mammals both in a complex – "the amazing food cooked by nature" (after Academician, Nobel Laureate, our great compatriot Ivan Petrovich Pavlov) and in the form of special drugs. The peptides are mentioned above. The hydrolyzates of milk proteins – casein and serum proteins are known as medical drugs and also as baby, dietary and special foodstuffs [57].

To our great regret, these unique products are contraindicated for a part of "Homo-Sapiens" because of anomaly (allergy) and painful symptoms (to death). Therefore, the vital problem is the receipt of special foodstuff for this small but existing in the human civilization of inhabitants of our planet Earth group of newborns. It is this noble aim that the researches of O.O. Babich were devoted to [20]. Specifically, the subject was concentrated on "the poison for suffering newborns with a genetic anomaly" – phenylalanine. The diagnosis of physicians – phenylketonuria - is a trouble for the kid and a signal to food industry workers – a special product of medical appointment is necessary. The modern Proteomics of dairy business implemented abroad provides the development of such product assortment. Now the scaling of results of researches of O.O. Babich allows to hope for real import substitution with domestic drugs. And Proteomics of dairy business, as an indispensable part of Laktoomics, replenished with a new, original section in which the information available in open publications in our country [38, 58] and abroad [59, 60, 61] is concentrated.

The informative part of researches [20] included the monitoring with the choice of special yeast Aureobasidium pullulans Y863 for the biosynthesis of enzyme L-phenylalanine-ammonium-lyase - PAL (EC 4.3.1.5), its immobilization on iron oxide nanoparticles using the method of tyophen acetylation with the receipt of industrial preparation which catalyzes the reaction of reversible deamination of L-phenylalanine to the compounds safe for the organism: trans-cinnamon acid and ammonia.

Fig. 8 and Table 9 provide the results of researches.

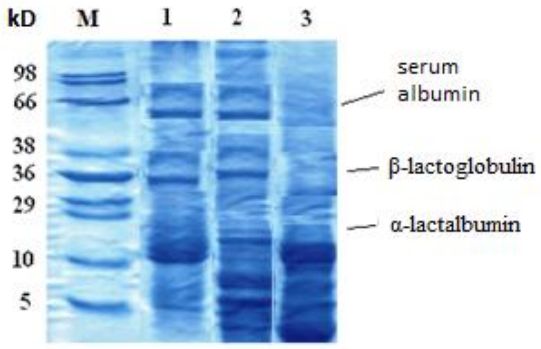


Fig. 8. Electrophoregram of enzymatic hydrolyzate of whey proteins with the different duration of hydrolysis: 1 – 30 min, 2 – 60 min, 3 – 90 min. M is a marker Roti-Mark Standard, 5–98 kD (Carl Roth, Germany).

Table 9. Characteristic of hydrolyzates of serum proteins, %

Parameter	Level of hydrolysis, with the duration of, min		
	weakly, 30	moderately, 60	deeply, 90
Percentage of split proteins in the hydrolyzate:			
α-lactalbumin	11.3 ± 0.6	45.5 ± 2.3	98.3 ± 4.9
β-lactoglobulin	5.6 ± 0.3	28.7 ± 1.4	77.1 ± 3.8
bovine serum albumin	0	13.9 ± 0.7	58.4 ± 2.9
Percentage of fraction with the molecular weight of <500 D	6.8 ± 0.3	12.4 ± 0.6	63.4 ± 4.7
Ratio of α-amino and total nitrogen	3.5 ± 0.2	8.8 ± 0.4	60.2 ± 3.0

With an increase in the depth of hydrolysis (it is regulated by the duration of process) the percentage of split proteins in a serum hydrolyzate increases, and it is the fermentolysis of α-lactalbumin that occurs most intensively. The rational parameters of controlled enzymatic hydrolysis of serum proteins using the complex of endo- and exopeptidases are the following: the temperature is 50 ± 1°C; the duration is 90 ± 1 min.; the enzyme-substratum ratio is 1 : 25.

The complex of experimental and theoretical researches served as a prerequisite for the creation of new types of specialized foodstuffs with the use of L-phenylalanine-ammonium-lyase. The technology includes the enzymatic processing of raw milk using the enzymatic system consisting of endo- and exopeptidases for the purpose of the maximum removal of phenylalanine from a polypeptide chain with the subsequent biotechnological processing of L-phenylalanine-ammonium-lyase providing the biotransformation of phenylalanine into the compounds which do not have a toxic effect on the patient's organism, and, thereby, the reduction of its content in a dairy equivalent up to 0.001%. This dairy equivalent can be the basis for the creation of a number of specialized dairy products for patients with phenylketonuria (dairy and protein ones and others). It is realized in 17 innovative developments the novelty of which is confirmed with patents for inventions. The technological developments are approved at the Institute of Molecular Biology (IMB) of the National Academy of Sciences of the Republic of Armenia (NAS RA), CJSC Khladotekhnika, Federal State-Funded Educational Institution of Higher Vocational Education "National Research Tomsk Polytechnic University" and introduced into production on a large scale in England by ClusterNanoTech LTD, in the way of transfer of technologies according to a license interstate agreement. The Russian Pentidomics of milk has come to the international level.

It means necessary now, within Proteomics, to consider briefly the original innovation which has appeared in recent years – the **MICRO-PARTICULATION** of milk proteins. In principle, this is the realization of postulates of nanobiotechnology in relation to a concrete natural object of researches. In the logic of historical development it is necessary to begin with the microparticulation of whey proteins.

The microparticulation of serum proteins began in 1984 with a US patent of the Canadian inventors N.S. Singler, Sh. Yamomoto and D. Latell on the product Simplesse [62]. The early system researches on the subject in our country were performed by Professor I.A. Smirnova in Kemerovo Institute of Food Science and Technology at the school of the master of cheese making, Professor L.A. Ostroumov. In the work by S.V. Manylov [63] the product of microparticulation of serum proteins Simplesse-100 was used in the production of cheeses and cottage cheese as the normalizer of initial mix with a positive effect. The system researches on receiving nanotubes on the basis of UV-concentrate of proteins of cheese whey are performed in Voronezh State University of Engineering Technologies for receiving the flavor (substitute) of milk by N.A. Podgornyy under the supervision of Professor E.I. Mel'nikova [64]. Fig. 9 provides the logical sequence of the technological line of receiving microparticulates of serum proteins (nanotubes), offered by the researchers, with the size of 1–3 microns.

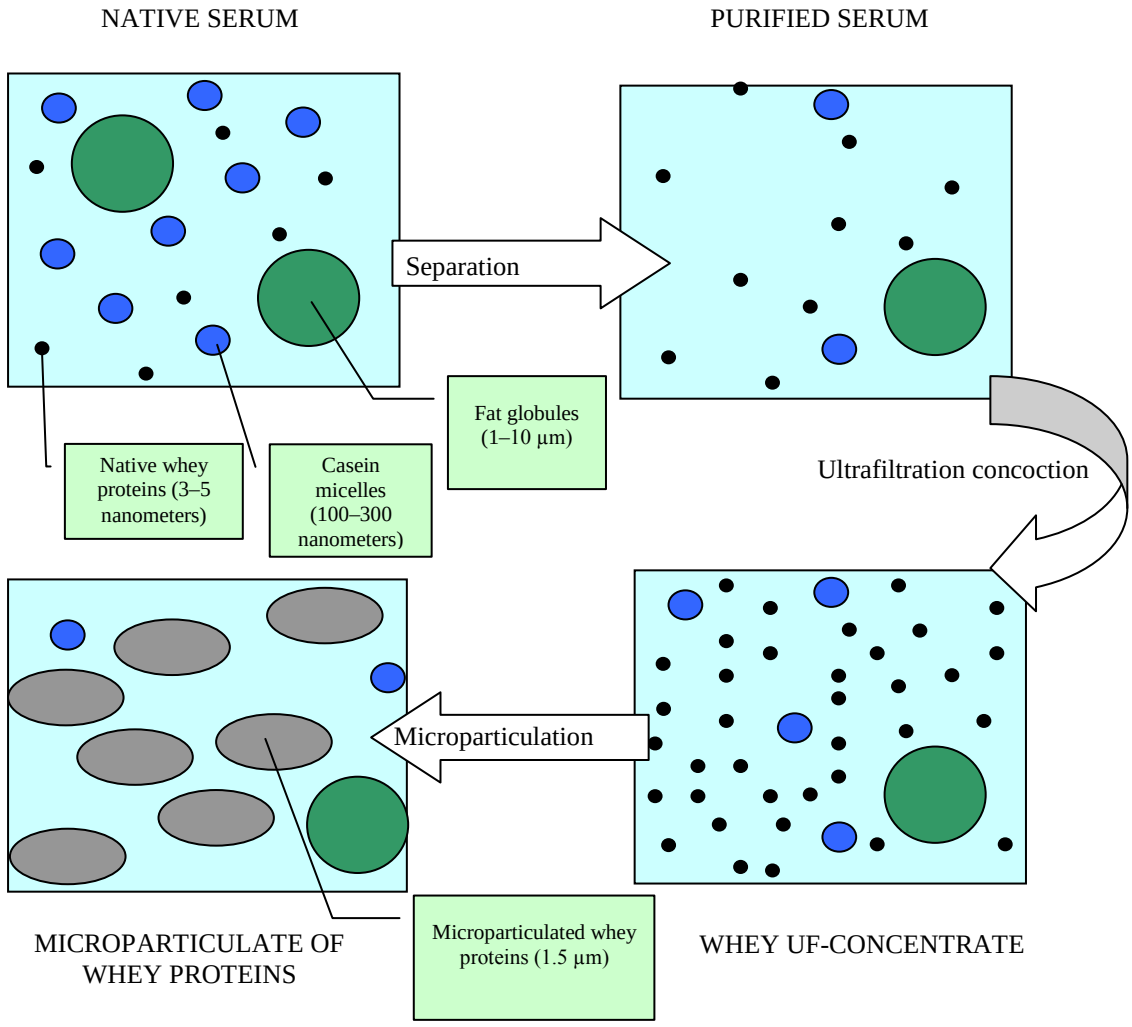


Fig. 9. Scheme of microparticulation of cheese whey proteins (according to E.I. Mel'nikova and N.A. Podgornyy).

The researches on the subject of microparticulation of synthesis of nanotubes of associates of serum proteins are actively performed by a lot of project teams, including our North Caucasus Federal University. I am sure that we expect exclusively interesting and positive results of the use of the so-called albumin milk (the former food means at distress prices) in the supertechnologies of products of functional purpose of the brand "NanoFood-NanoEda". This is a bright confirmation of the phenomenon of derivatives of components of serum at the cluster level of fractal supertechnologies.

The casein microparticulates are received in the work by V.K. Shtrigul' [65] under the supervision of Professor I.A. Smirnova (continuity of problems) in Kemerovo Institute of Food Science and Technology, which does credit to the creative team of scholar school of Professor L.A. Ostroumova and Rectror of the institute, Professor A.Yu. Prosekov.

The informative part of innovation included the search of the optimum way to "force" casein micelles to be aggregated in the nanotubes imitating the flavor of milk fat. Of the four tested variants known and used in the branch – thermal acid, acid, chlorcalcic and rennet coagulations, not the best (chlorcalcic coagulation has a bitter flavor) but a rational one was chosen – rennet coagulation. The "perk" of the process, which is schematically shown in Fig. 10, is the stage of interruption of complex formation of casein micelles at a certain stage ("know-how") – shown in the form of a road sign.

For the realization of process of interruption of complex formation of casein micelles a simple, but original operation – disoxidation up to pH 7.0 using alkaline solution of caustic sodium is used. Casein micelles, at the same time, reach the level from the initial (native) size of 40–300 nanometers to 1 micron and can imitate a flavor of milk fat after the thermal treatment combined with pasteurization, and controlled dispergating. Objectively, the jellification process (trivially – souring) is visible in case of change of viscosity of the system.

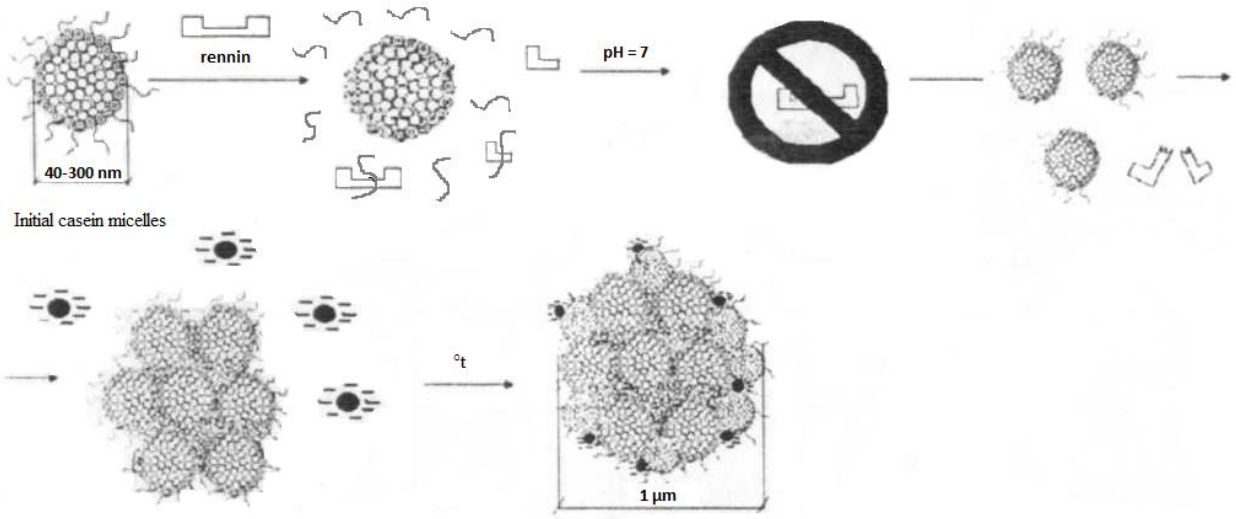


Fig. 10. Hypothetical scheme of the process of logistics of microparticulation of casein of raw milk (according to I.A. Smirnova and V.K. Shtrigul').

A line of dairy drinks of new generation is realized on the basis of casein microparticulates. The received low-fat products had a distinct creamy taste due to the flavor of milk fat of microparticulated casein (nanotubes). The stage of microparticulation organically fits in the technological process of production of traditional dairy drinks. The information about the innovation of Kemerovo Institute of Food Science and Technology is the real embodiment of high (critical) nanobiotechnologies of Laktoomics in the dairy industry, already using the example of casein Proteomics.

CONCLUSION. INNOVATIVE PRIORITIES

All the above concerns the Proteomics of dairy business and gives the grounds for the formation of paradigm of Technological Platforms of modernization of dairy industry of the agrarian and industrial complex, as a component of the food industry, at the level of the sixth technological mode – supertechnologies.

The formation of Proteomics, including that of Peptidomics and dairy business according to product line groups and individual products shall include the study of casein Genomics by cattle breeders at the stage of synthesis in the alveoli of udder of lactating female of mammals with the controlled regulation of content and ratio of fractions, and also of genetic variations. At the same time, the dairy industry with the implementation of principles of chremostatics (profit economy) shall be as the customer.

The use of the optimized model of protein complex of raw milk in products with the complete use of components, their extraction and the receipt of necessary derivatives is the prerogative of dairy industry of agrarian and industrial complex, according to the provisions of the existing food theory and the recommendations of professional nutritionists.

The critical (high) technologies of complex of milk proteins, caseins and whey proteins are well-known and correspond to the fifth technological mode – the principles of biotechnology.

The innovative supertechnologies (the sixth technological mode – nano- and pico-) are implemented in a biogenetic paradigm – complex formation, hydrolysis, proteolysis; molecular size-exclusion filtration (membrane technologies) and microparticulation. Scaling concerns dairy and milk-containing bioecoproducts of the "green basket" of functional, dietary (healthy) and clinical nutrition.

In loving memory of my dear curator, an opponent
to my Candidate's and doctoral dissertations,
Professor Pavel Fedorovich D'yachenko
who made an invaluable contribution to the proteomics of milk proteins

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