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POTENTIAL OF USING *SACCHAROMYCES BOULARDII* TO PRODUCE FERMENTED MILK PRODUCTS

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Abstract. The analysis of the literature allows us to characterise the potential of the new probiotic yeast strain *S. boulardii*. The paper describes the long period of formation of fundamental knowledge and introduction of some technological methods into the production of different fermented milks products. Besides the historical aspect, the microbiological diversity of fermented milks products is considered, and the technological differences in manufacturing them are shown. It is known that yoghurt is one of the most famous fermented milk products. This dairy product has been very popular for years due to its taste characteristics and ease of manufacture. With the accumulation of knowledge about probiotics and the yoghurt production technology, there has appeared a tendency to further enrichment of the product with certain probiotics, prebiotics, and minerals. Today, yoghurt manufacturing actively uses the method of enriching the finished product with probiotics. This allows creating a qualitatively new functional food product that not only has nutritional value for the consumer, but also produces a certain positive effect on intestinal microbes and thus on the consumer's health. Bacteria are known to be the main probiotics, but the recent discovery of the probiotic properties of certain genera and species of yeast opens up new prospects of their use, both in the pharmaceutical industry and in creating functional foods. The recently discovered yeast strain *S. boulardii*, phylogenetically related to *S. cerevisiae*, has many therapeutic effects and significant advantages over bacterial probiotics, in particular, it is resistant to antibiotics. *S. boulardii* is a probiotic strain that can be used to enrich yoghurt. The physiological properties of the strain and therapeutic properties of the products of its metabolism along with the technological parameters of yoghurt processing make a combination of the probiotic and this beneficial fermented milk very promising. It has been determined that to produce enriched yoghurt, it is possible to use both a lyophilised culture of *S. boulardii* and a microencapsulated one. On analysing the economic aspect, especially the sale of yoghurts and the further tendency towards an increase in its consumption, we can say that the introduction of *S. boulardii* as an enrichment strain is a promising issue of current importance.

Key words: yeast, yoghurt, probiotics, biotechnology, functional food products, food technologies.

Introduction. Formulation of the problem

Milk and various dairy products are known for their nutritional and functional value and are considered an integral part of a healthy diet [1]. It is believed that fermented dairy products appeared by chance, and so did such products as kefir and plain yoghurt (the most commonly used fermented milk products today), which were the result of fermentation in bags made of animal skins used to transport milk [2]. It should be noted that the production of fermented food and beverages, including dairy products, and knowledge about probiotics has evolved since the emergence of man as a species [2, 3]. Certain dairy products, such as cheese, butter, and fermented milk products, are known to have been produced since at least 3,000 BC.

However, the industrial processing of milk for the production of dairy products dates back to the mid-nineteenth century [4], i.e., to the time when microbiology began developing as a scientific and practical field. It was then that an interest in various dairy products increased, which was due to Louis Pasteur's discovery of the microbial nature of fermentation and Ilya Mechnikov's establishing the relationship between lactic acid bacteria and longevity [2]. The discovery of different types of lactic acid bacteria and bifidobacteria gave impetus to the study of their potential benefits to humans, which, in turn, contributed to the development of the dairy industry and biotechnology of probiotics [3,5].

Today, the dairy industry is one of the most organised and developed sectors of the food industry. There is a wide range of products on the market to satisfy any consumer's taste, such as yoghurt, kefir, sour cream, milk, cheese, butter, etc. [6]. Usually, in the dairy industry and in the production of starter cultures, the following representatives of the genera of probiotic microorganisms are used: *Lactobacillus*, *Bifidobacterium*, *Saccharomyces*, and *Streptococcus* [4].

Biotechnological advances in recent years have become a powerful tool for the development of quality characteristics of dairy products and the introduction of "advanced" products such as lactose-free products, functional foods, and dairy products with additional probiotic enrichment [7,8]. Probiotic is a functional food ingredient in the form of useful non-pathogenic and non-toxicogenic living microorganisms. When used systematically in the form of drugs or in food, it has a beneficial effect on the human body by normalising the composition and increasing the biological activity of normal intestinal microbiota [9].

Another important achievement of modern microbiology and biotechnology is the creation and production of starter cultures. The steady growth of the dairy market [10,11], increasing research on probiotics and functional foods, and consumers' interest in products that have both nutritional value and positive health effects make it necessary to create new types or names of dairy products [4,7,10,11]. The positive dynamics of changes in the annual number of publications (Fig. 1) on "probiotic" and functional foods is convincing evidence of the growing interest of scientists and dairy producers in increasing and updating their range.

According to the graphs, the first publications on functional foods appeared in the PubMed scientometric database in 1911, but a significant increase in interest in the subject began in the mid-1970s. The largest number of publications, as of early 2021, is observed in the Web of Science database. On "probiotics," the first publications in this database appeared in the mid-1970s, and significant growth began in the mid-1990s. The largest number of articles on the subject "fermented dairy products" is available in the scientometric database Scopus.

The most popular and most used dairy products (and most useful for maintaining a normal microbiota of the gastrointestinal tract) include a variety of yoghurts. Yoghurt is a fermented milk product that contains certain viable non-pathogenic strains of bacteria, usually *Streptococcus thermophilus* and *Lactobacillus bulgaricus* [12]. Yoghurts are the most popular food carriers of probiotic properties. The forecast research by Bridge Bridge Market Research has shown that the yoghurt market will grow in the period from 2021 to 2028 by an average of 4.80 % per year [13].

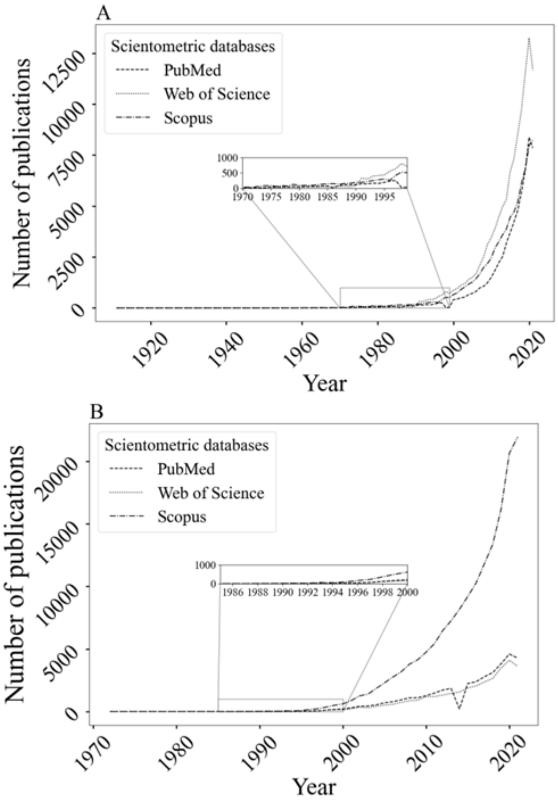

Fig 1. Analysis of publications on the following topics: A – "functional foods"; B – "probiotics" (based on data of PubMed, Web of Science, Scopus)

The use of fermented dairy products in food as a source of probiotic microorganisms with a therapeutic effect is a very new and promising idea. Today, there are products that, in addition to those listed above, use such well-known probiotic strains as *L. acidophilus*, *L. lactis*, *L. bulgaricus*, *L. casei*, *B. breve*, *B. lactis*, *St. thermophilus*. However, the discovery, description, and comprehensive biological research on a new strain of yeast *S. boulardii*, have made it possible to use it to produce a qualitatively new fermented milk product that will combine nutritional and therapeutic properties.

The purpose of the work is to analyse modern scientific literature with prospects of creating a new functional fermented milk product in combination with the probiotic yeast *S. boulardii*. The paper aims at analysing systematically the probiotic properties of the yeast strain *S. boulardii*, the technological features of fermented dairy production, and historical aspects of dairy production.

Analysis of recent research and publications

Development of knowledge in the field of fermented milk products and probiotics

Today, milk and dairy products are common in many countries around the world. It is believed that fermentation of dairy products is one of the oldest methods used to increase the shelf life of milk. The exact date and place of the first production of dairy products cannot be established. However, there are historical studies that show more than ten thosands years of experience in making dairy products in the form of fermented milk, associated with changes in the lifestyle [14,15], in the type of livestock, and in agriculture in primitive life at an early stage of human development.

Dairy farming and consumption of dairy products became common among prehistoric farmers, primitive hunters and collectors who used pottery. According to certain archeological studies, parts of ceramic products were found in the Early Neolithic sites in Europe, which are today interpreted as a "cheese sieve" [16,17]. Mass spectrometric analysis of tartar from the remains of the Bronze Age shows direct protein evidence of consuming cow's, sheep's, and goat's milk in seven of nine individuals. It is believed that dairy farming was quite common in the eastern steppes, i.e. within modern Eastern Europe, Mongolia, and the Altai-Sayan mountain country [18].

Since the emergence of dairy farming, people have discovered the nutritional value of milk and the possibility of producing granular milk cheese, which has a longer shelf life and, consequently, longer terms of consumption. The production of the first fermented milk products about 8,000 years ago is evidenced by the sculptural relief in Tel el-Ubayda dating back to ancient Babylon. There is other historical evidence for the use of various products made from milk, for example, Hippocrates' mentions of the nutritional and therapeutic benefits of milk [14], Pliny the Elder's records of the benefits of fermented milk [2,3]. The use of such fermented milk products as kefir, koumiss, matzoon, leben, tan and others was widespread by nomadic and semi-nomadic tribes [2,14]. In general, more fermented milk drinks appeared in the east, in the mountains of the Caucasus, Turkey, and Central Asia. The appearance of the famous drink kefir dates back to about 1 thousand years ago and is associated with the legend of the gift of the prophet Muhammad [19]. The first fermented milk products, or their prototypes, were created by accident, due to spontaneous fermentation of milk by various bacteria when it was contained in bags for storage [2,14,20].

Yoghurt was mentioned in the 11th century AD. It was described by Yusuf Hass Hajib Balasaguni in the famous book Kutadgu Bilig [2,12,14]. This mention shows the use of yoghurt to prevent or treat gastrointestinal diseases [2]. A critical stage in the formation of knowledge related to dairy products and probiotics was the study of microorganisms in fermented milk or plain yoghurt. This observation was made by Andri in 1701 [21,22]. Despite the available therapeutic and nutritional properties, as well as the long history of various lactic acid products, these products were manufactured locally and did not have a global distribution [14].

Only with the development of microbiology and research of microorganisms contained in dairy products, it has become possible to scale up and standardise the process of dairy production. The key to it was the creation and commercial production of starter cultures, which are the "heart" of fermented milk products – components of high quality fermented dairy products [23].

Significant discoveries and the impetus for increasing knowledge about dairy products and the microorganisms contained in them came after the research by Joseph Lister, Louis Pasteur, and his students, Stamen Grigorov and Ilya Mechnikov.

It was Pasteur and his successors who contributed most to the general development of microbiology and its branches, including the so-called dairy biotechnology. Lactic acid-producing bacteria were first discovered by Pasteur in 1857 [14]. In 1880–1888, scientists at the Pasteur Institute isolated lactic acid bacteria from the human gastrointestinal tract [2]. Another important achievement of Louis Pasteur was the creation of a method of destroying most spore-forming bacteria by heating, which was called pasteurisation. Today, this method is actively used in the production of milk and dairy products [4,14].

Later, after the discovery of Pasteur's methods of pure cultures, in 1873, Joseph Lister isolated pure cultures of lactic acid bacteria from curdled milk. They were called *Bacterium lactis* [22,23]. Lister's discovery allowed the development of so-called starter cultures from pure cultures or combinations thereof [15,23]. It was not until the late 1880s that Storch in Denmark, Weigman in Germany, and Conn in the United States proved that pure cultures and starter cultures could be used to make a variety of dairy products, such as cream. Methods of standardisation of sour cream butter based on the introduction of starting cultures were developed [23,24]. Along with these discoveries, Christian Hansen started his business of producing starter cultures for various industries, including dairy [24].

In parallel with the first successes in producing starter cultures and the introduction of industrial manufacture of fermented milk products, the question of the benefits and therapeutic properties of fermented milk products was raised. The study of microbiota of fermented milk products and their therapeutic properties formed the idea of beneficial microorganisms – probiotics. Thus, one of the first scientists to suggest the idea of health benefits of consuming lactic acid products, namely yoghurt, was the Bulgarian medical student Stamen Grigorov.

Grigorov was the first to discover the microorganism *Bacillus bulgaricus* (today *L. bulgaricus*), that is still used in starter cultures for yoghurts [12,22]. Based on Grigorov's work, in 1909, Nobel Laureate Ilya Mechnikov suggested the idea of the benefits of yougurt lactobacilli and the relationship of longevity of the Bulgarian population with the consumption of such fermented milk products [22]. These studies have made a significant contribution to the promotion of dairy products, including yoghurt. It should be noted that studies of other lactic acid products were conducted too. In general, at the end of the XIX century not only yoghurt but also koumiss and kefir were studied. Thus, it is known that kefir was effectively used in tuberculosis sanatoria, and in European countries it was used as a tonic drink [5].

Already in the early twentieth century, due to its therapeutic and taste properties, yoghurt became a commercially important product. Its production was started by the businessman from Barcelona Isaac Carasso. His son founded Danon later [2,22]. During the period 1910–1920, microbiologists isolated and prepared various pure cultures for the production of fermented milk products [23,24]. Further development in the industrial manufacture of these products consisted in introducing new promising strains of microorganisms isolated from different natural sources, as well as in studying probiotic properties of new strains and creating products based on them, valuable both nutritiously and therapeutically [25]. One of the most striking examples of the introduction of the therapeutically valuable and promising microorganism *L. casei* Shirota is the Japanese product *Yakult* [14,15]. The summarised history of research on fermented milk products and microorganisms is given in Table 1.

Table 1 – Chronology of scientific and technological research into fermented milk products

Year	Author of research	Discovery	References
1	2	3	4
1701	Andri	The presence of microorganisms in sour milk	[21, 22]
1780	Carl Wilhelm Scheele	Study of lactic acid	
1855	Pierre Jacques Antoine Bechamp	Study of sucrose inversion by microorganisms	[21]
1857	Louis Pasteur	Biosynthesis of lactic acid by microorganisms	
1862	Louis Pasteur	The invention of pasteurisation	[14]
1868	Senator	Protein breakdown in the gastrointestinal tract can cause toxemia	[14, 26]
1873	Joseph Lister	Description of *Bacterium lactis* (modern *Lactococcus lactis ssp. lactis*)	[21, 22]
1874	Christian Albert Theodor Billroth	Development of the theory of intestinal intoxication	
1883	Mykola Sorokin	The study of bacteria and fungi of kefir	[5]
1884	Charles Jacques Bouchard	Development of the theory of intestinal intoxication	[14, 22]
1886	Ortweiller	Demonstration of the therapeutic effect of consuming certain carbohydrates	
	Hirschler	Demonstration of the effect of sucrose, lactose, dextrin consumption on inhibiting intestinal putrefaction	
	Theodor Escherich	Studying bacteria in the gastrointestinal tract of children, the discovery of *Bacterium coli* (modern *Escherichia coli*)	
1892	Albert Sigmund Gustav Döderlein	Determining the role of lactic acid bacteria in the treatment of gynaecological diseases	
1893	Christian Ditlev Ammentorp Hansen	The first production of starter cultures for fermented milk products	[27]
1900	Henri Tissier	Description of bifidobacteria	[2, 14, 22]
	Ernst Moro	Description of *B. acidophilus* (modern *L. acidophilus*)	[14, 22]
1903	Henri Tissier, Pascal Gasching	Demonstration of inhibition of growth of putrefactive organisms by acid-forming bacteria	[14]
1904	Weiss	Demonstration of the presence of large amounts of *B. acidophilus* (modern *L. acidophilus*) in the human intestine after consumption of milk	[14]
1905	Stamen Grigorov	Description of *Lactobacillus bulgaricus*	[2, 21, 22]
1907	Ilya Mechnikov	Publication of *The Prolongation of Life: Optimistic Studies* and the emergence of the idea of a relationship between lactic acid bacteria and longevity	[21, 22]
1919	Orla-Jensen	Description of *Streptococcus thermophilus*	[14, 22, 28]
	Isaac Carasso	Establishment of a yoghurt laboratory and Danone	[2, 14, 29]

Continuation of table 1

1	2	3	4
1921	Leo F. Rettger та Harry A. Cheplin	Description of the therapeutic properties of *B. acidophilus* (modern *L. acidophilus*)	[14, 30]
	Orla-Jensen	Study of the symbiosis of fermentation starters for yoghurts and other fermented milk products	[14]
1932, 1935	Leo F. Rettge	Additional description of the therapeutic properties of *L. acidophilus*, introduction of the production technology of acidophilic milk	[14, 22, 31]
1933	–	The first addition of fruit to yoghurt	[22]
1935	Minoru Shirota	Development of the *Yakult* fermented milk product containing the probiotic strain *Lactobacillus casei* Shirota (according to the current classification *Lacticaseibacillus casei*)	[2, 10, 22, 32]
1950	Pette, J. W., Lolkema, H.	Discovery of symbiosis in the mixed cultures of *Lactobacillus bulgaricus* and *Streptococcus thermophilus*	[21, 22, 33]
		Description of acetaldehyde as a compound associated with the aroma of yoghurt	[22]
1960	J. C. de Man, M. Rogosa, M. E. Sharpe	Creation of MRS agar used for the growth of lactobacilli	[22]
1973	G. V. Reddy, K. M.	Investigation of the inhibitory effect of yoghurt on the proliferation	[22, 34]
	Shahani, M. R. Banerjee	of Ehrlich ascites carcinoma tumor cells	
1974	George V. Mann, et al.	Detection of a new therapeutic effect of fermented milk products: lowering cholesterol levels when consuming fermented milk	[22, 35]
1975	B. E. Terzaghi, W. E. Sandine	Creating the growth medium M17 for growing lactococci	[22, 36]
	M. Kalab, D. B. Emmons, A. G. Sargant	Study of the microstructure of yoghurt	[22, 37]
1985	–	Lactose-free milk, ice cream, and yoghurt production technology was developed	[38]
1987	–	Creating yoghurt with *Bifidobacterium animalis* DN-173 010	[22]
1989	Sherwood L. Gorbach Barry R. Goldin	Patenting the strain *Lactobacillus rhamnosus* GG	
1994	–	Creation of a dairy product containing *L. casei* DN-114001 or *L. casei* Immunitas	
1995	Robinson Richard K.	Adding inulin to yoghurts as a prebiotic and bifidogenic factor	[22, 39]
2014	Anbukkarasi *et al.*	Development of yoghurt with a low galactose content	[22, 40]

The use of pure cultures of lactic acid-producing microorganisms, the production of starter cultures based on them, the study of probiotic properties of microorganisms, and the further development of so-called "milk" microbiology have made the manufacture of fermented milk products more advanced [41,42]. Information and research on the therapeutic properties of bacterial products isolated from dairy products have initiated the modern trend of creating functional dairy foods [25,43]. Functional foods are foods that are part of a normal diet and, along with nutritional properties, have a positive effect on various body functions, which reduces the risk of chronic diseases, if these products are consumed regularly [44,45].

In general, different fermented milk products require special production conditions, which are associated with the use of different producers and optimal growth conditions for them, i.e. require the use of different technologies. The use of specific producer strains of a particular fermented milk product depends on obtaining the desired characteristics: taste, smell, appearance, and consistency [24,46]. Modern fermented milk products are yoghurts, sour cream, acidophilic milk, kefir, koumiss, etc. [4]. Microorganisms used as yeast in the production of fermented milk products, temperature conditions, and specific features of the technological process are shown in Table 2.

According to these historical and scientific data, yoghurt is the most studied and consumed fermented milk product [22]. This product has the largest number of product forms that differ in taste and texture [4,22]. The classification of yoghurt by product forms and methods of production is shown in Fig. 2.

Today, most of the bacteria that are part of starter cultures, especially certain production strains, are probiotics with many therapeutic properties [51]. Especially in recent decades, there has been a tendency towards the creation of probiotic-enriched and functional fermented milk products [25, 52]. Most often, yoghurt is considered as a "base," or probiotic-enriched food product. Compared with other fermented milk products, yoghurt has significant advantages that indicate the possibility of enrichment with probiotics: availability, nutritional value, increased survival of bacteria, ease of inclusion in the daily diet [51]. Yoghurt is also a sought-after product highly regarded by consumers due to its health benefits that make it the most promising for further development of a new range of fermented milk products [53].

Table 2 – Fermented milk products, starter cultures, and technological parameters of production

Product	Type of milk	Starter culture	Fermentation type	Fermentation		Shelf life (4°C)	pH of the finished product, units	References
				Temperature, °C	Time, hours			
Yoghurt	Cow's milk	*Lactobacillus acidophilus* *Streptococcus thermophilus* *Lactobacillus delbrueckii ssp. bulgaricus*	HM HM HM	41–45	2–5	2–3 weeks	4.0–4.4	[46, 47]
Kefir	Sheep's, cow's, goat's, or mixed milk	*Lactococcus* *Lactobacillus* *Leuconostoc* *Lentilactobacillus kefiri* *Acetobacter* Yeast	HM HM HT HT – –	20	24	10–14 days	4.3–4.5	[46, 47]
Sour cream	Cow's milk	*Lactococcus lactis* ssp. *lactis*	HM	22	16	25–45 days	4.5	[47, 48]
		Leuconostoc mesenteroides	HT					
Koumiss	Mare, camel, or donkey milk	*Lactobacillus* Non-lactose-fermenting yeast	HM –	27	2–5, cool ageing	10–14 days	3.0–3.5	[46, 47]
Crème fraîche	Cow's milk	*Lactococcus lactis* *Leuconostoc mesenteroides*	HM HT	20	15–20	10–30 days	4.5	[47]
Buttermilk	Buffalo or cow's milk	*Lactococcus lactis* ssp. *lactis* *Lactococcus cremoris* *Leuconostoc mesenteroides* ssp. *dextranicum*	HM HM HT	22	14–16	10 days	4.4–4.8	[46, 47]

*HM – homofermentative lactic acid fermentation, HT – heterofermentative lactic acid fermentation

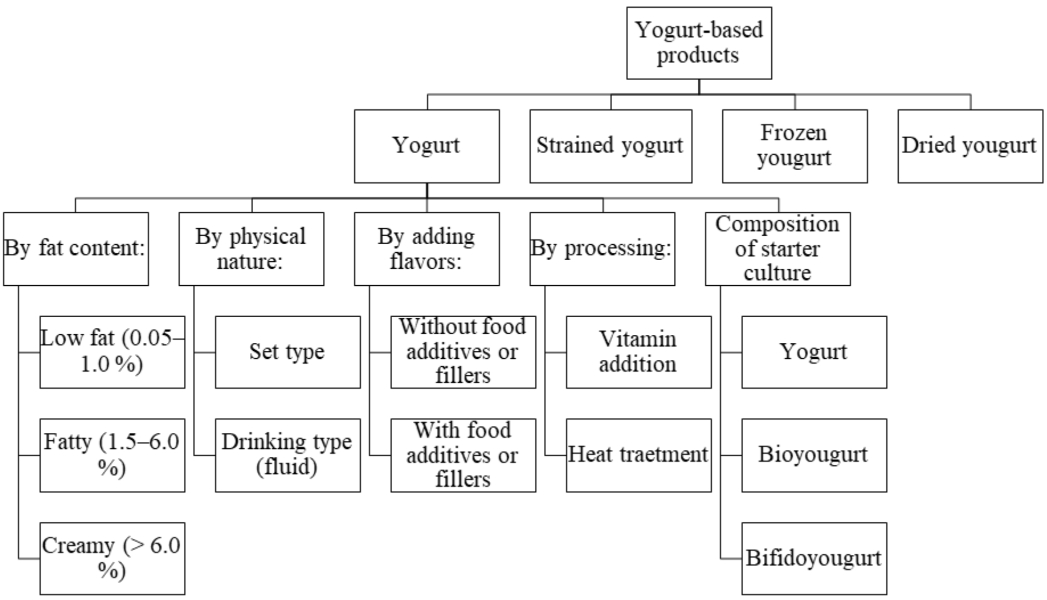

Fig. 2. Classification of products based on yoghurt [49,50]

We can say that the first therapeutically valuable product was *Yakult*, manufactured by Yakult Honsha, Japan [22]. The fermented milk product contained the strain *Lactobacillus casei* Shirota [22,54], or, according to the current classification, *Lacticaseibacillus casei* Shirota [55]. There is extensive experience in adding extra probiotic strains to standard yeast, such as *Lactobacillus acidophilus* and *Bifidobacterium bifidum* [12].

Although yeast is usually part of the normal microbiota of fermented milk products [56], only a few decades ago, the first studies on the probiotic properties of certain species appeared [57]. The main studied and therapeutically valuable eukaryotic probiotic strains are: *Saccharomyces cerevisiae*, *Saccharomyces boulardii*, *Kluyveromyces lactis*, and *Kluyveromyces marxianus* [51,58].

Functional characteristics of S. boulardii

Today, the dairy industry uses a large number of prokaryotic, namely bacterial strains of probiotics, such as the genus *Bifidobacterium* or the family *Lactobacillaceae*. However, in recent decades, more and more attention has been paid to eukaryotic microorganisms with probiotic properties, which may be promising in manufacturing certain products [57,59]. Among the representatives of eukaryotic probiotic strains, one of the most studied strains of yeast is *Saccharomyces boulardii*, or *S. cerevisiae* var. *boulardii*. It is a tropical strain of yeast, first isolated from nephelium and mangosteen fruit in 1923 by the French scientist Henri Boulard. This species is related to brewer's yeast (*S. cerevisiae*) in its taxonomic and metabolic characteristics. *S. boulardii* maintains and restores the normal intestinal flora and is therefore classified as a probiotic [59,60].

Henri Boulard first isolated this yeast after observing that Northeast Asians often chewed fruit (for example, mangosteen) to suppress cholera symptoms. It has been shown that *S. boulardii* is not pathogenic, remains in the digestive tract, and grows at unusually high temperatures – from 37°C. Lyophilised *S. boulardii* cells are used as a probiotic to treat and prevent of diarrhoea. The lyophilisate of these cells has antimicrobial and antitoxic action against bacterial cyto- and enterotoxins, increases the intestinal enzymatic function, has natural resistance to antibiotics, passes through the digestive system unchanged without colonisation, and is completely eliminated from the body within 2–5 days after its intake is finished [61,62].

The strain was later found in tea fungus and in some fermented milk products, such as kefir [59].

According to the cell morphology of *S. boulardii* (oval or spherical cells 2–3 μm wide and 2.5–10.5 μm long [59]), it has a thicker cell wall, as compared with *S. cerevisiae* [59,63].

Initially, the microorganism was classified as a new species in the genus *Saccharomyces* [64], due to its physiological features and differences from *S. cerevisiae*.

Unlike *S. cerevisiae*, *S. boulardii* has the following characteristics: inability to produce ascospores, transition to haploid form, better resistance to high temperatures and acid stresses [65,66].

Despite some controversy about the taxonomic position, current molecular studies indicate that *S. boulardii* is still a strain of *S. cerevisiae*, the current taxonomic affiliation of *S. boulardii* is shown in Table 3 [61,67,68].

Table 3 – Current taxonomic position of *S. boulardii* [69]

Domain	***Eukaryota***
Kingdom	*Fungi*
Subkingdom	*Dikarya*
Phylum	*Ascomycota*
Subphylum	*Saccharomycotina*
Class	*Saccharomycetes*
Order	*Saccharomycetales*
Family	*Saccharomycetaceae*
Genus	*Saccharomyces*
Species	*Saccharomyces cerevisiae*
Strain	*Saccharomyces cerevisiae* var. *boulardii*

Scientific and practical interest in eukaryotic probiotics in general is growing every year. The dynamics of this growth reflected in the number of publications for the query "*Saccharomyces boulardii*" is shown in Fig. 3.

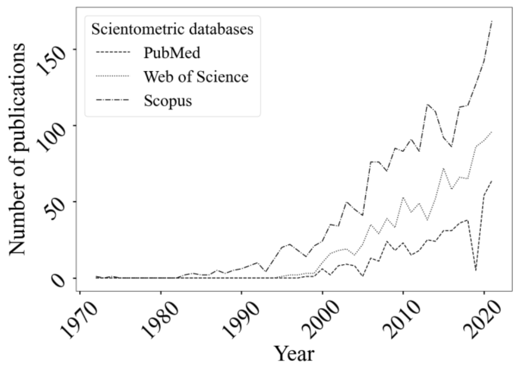

Fig. 3. Number of publications by year for the query "*Saccharomyces boulardii*" (based on data of PubMed, Web of Science, Scopus)

As can be seen from the figure, the number of scientific publications on the query "*Saccharomyces boulardii*" has been growing in the last 20 years. Most of the new publications are recorded in the Scopus scientometric database, but the number of new scientific papers is increasing in the Web of Science and PubMed databases.

Certain studies using ITS-PCR, microsatellite fingerprinting, and genome sequencing indicate the presence of enzymes involved in the Leloir pathway, i.e. galactose utilisation [68], although prior to the detection of enzymes in this pathway, *S. boulardii* was considered to have no galactose utilisation [64,66]. According to genome sequencing, *S. boulardii* has certain features: absence of Ty1-2 elements, trisomy on chromosome IX, absence of MAT alleles and NO genes, lack of spore formation due to respiratory deficit [61].

Despite the homology of the genomes of *S. cerevisiae* and *S. boulardii*, which is more than 95 %, *S. boulardii* still has high probiotic activity, as compared with *S. cerevisiae* [70]. This is achieved by an increased ability of pseudohyphal switching and better survival rates at acidic pH [67]. *S. boulardii* has been shown to secrete serine protease (54 kDa), phosphatase (63 kDa), and thermolabile and trypsinolabile nonproteolytic proteins (120 kDa), which protect the intestinal microbiota by cleaving endotoxins (e.g. *E. coli* [71]) or with the mechanism of decreasing in cAMP levels [61,68, 70]. Also, important parameters that characterise *S. boulardii* as a probiotic are stress resistance and survival under adverse conditions. The optimal growth temperature of *S. boulardii* corresponds to the human temperature 37°C [65]. Other studied probiotic properties of *S. boulardii* are resistance to digestive enzymes, limiting the growth of certain pathogenic bacteria (*Staphylococcus aureus* and *Pseudomonas aeruginosa*) through the synthesis of organic acids (caproic, caprylic), natural resistance to antibiotics, and the ability to grow on prebiotic carbon sources, e.g. fratufite (fructose with inulin) [59,66,72,73].

Today, due to its proven therapeutic properties, *S. boulardii* is considered a probiotic strain. Successful uses of this probiotic results in prevention and treatment of antibiotic-associated diarrhoea [59, 74], especially treatment of infections caused by *Clostridium difficile* [74,75]. The ability of *S. boulardii* to prevent infections associated with invasion of *C. difficile*, *E. coli*, and *Candida albicans* or their attachment to the cells of the gastrointestinal tract was reported [59,60,74,76]. Recently, antitumor effects of *S. boulardii* have been discovered. It was established that glucan extracts could have a prophylactic effect on tumors of the colon of rats [59]. There are also studies on the effectiveness of *S. boulardii* in travellers' diarrhoea and acute diarrhoea in children [71,76]. The use of *S. boulardii* in the prevention and treatment of *Helicobacter pylori* infection [77], irritable bowel syndrome [78], and acute gastroenteritis [79] was reported. Besides, it is known that *S. boulardii* can synergistically affect other probiotics of prokaryotic origin. For example, the compatible antipathogenic activity of *Lacticaseibacillus rhamnosus* GG and *S. boulardii* CNCM-I-1079 against the enteropathogenic strain *E. coli* LMG2092 was studied. The study found that a combination of probiotics could improve the functionality of the microbiota in both adults and children [80].

Most of the possible mechanisms of action of *S. boulardii* are still understudied. The main ones are: antimicrobial effect, inactivation of bacterial toxins, immunomodulatory effect, trophic effect, stimulation of producing short-chain fatty acids, polyamines, and digestive enzymes [62,81-83].

Today *S. boulardii* is available as a medicine in various dosage forms, the use of which is quite safe. However, an increase in infections and fungaemia has been reported in critically ill or immunodeficient patients [74,84]. Certain studies and meta-analyses [81, 85] indicate that, despite colonisation of the gastrointestinal tract by *Saccharomyces* spp., there are no cases identified of fungal sepsis caused by *S. boulardii*, so the microorganism is safe to consume for therapeutic purposes [74].

Technological features of yoghurt production. Possibilities of enrichment of yoghurts with S. boulardii

Due to the large number of therapeutic effects and nutritional value of *S. boulardii*, there are prospects of creating a functional dairy product with the addition of these microorganisms [86]. Due to the thermophilicity of the strain, its resistance to low pH, and symbiotic action on other probiotics, the possibility of integrating *S. boulardii* into various fermented foods has been considered for a long time [71]. Yoghurt is one of the most studied and best probiotic delivery systems [86].

Because of their diversity and popularity, there are a large number of types of yoghurt, but its technology is quite standardised [4]. The main differences in technology in the production of different types of yoghurt depend on the consistency. However, the main stages are common to all types [87]. The first stage is the selection and preparation of milk. The quality of the finished product will depend on the quality of the milk. Milk must be of the highest bacteriological quality, low in bacteria and substances that can prevent the development of yeast [88]. Microbiological contamination is usually removed by heat treatment [87]. After the primary processing of milk, it is standardised according to established technological parameters and homogenised [88]. Prepared milk is fermented by selected cultures (usually *L. acidophilus*, *L. casei*, *L. delbrueckii* ssp. *lactis*, *L. helveticus* ssp. *yoghurts*, *B. animalis* ssp. *lactis*, *B. longum*, *B. bifidum*, *B. infantis*, and *St. salivarius* ssp. *Thermophiles*). However, in accordance with international and regional law, there are requirements for the mandatory presence of *S. salivarius* ssp. *thermophilus* and *L. delbrueckii* ssp. *Bulgaricus* [4,87,88]. Fermentation is carried out at 45°C. After fermentation, the resulting product is cooled, and the finished product is packaged [87,88]. A simplified block diagram of the production of yoghurts of different types is presented in Fig. 4.

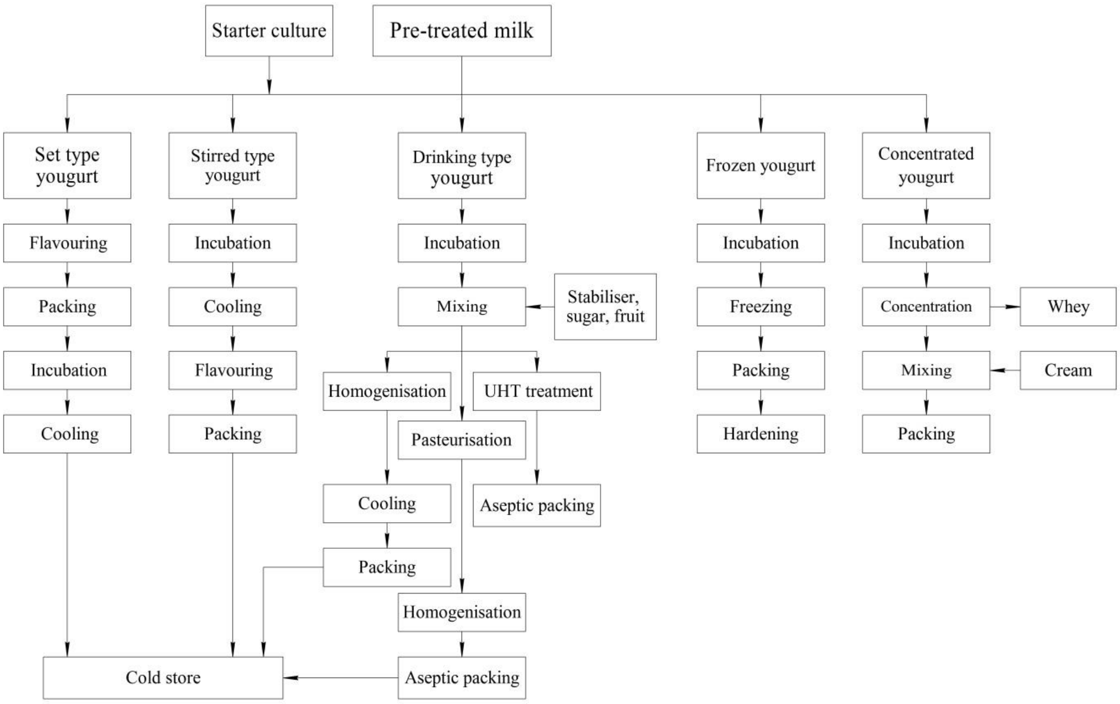

Fig. 4. Block diagram of production of different types of yoghurt [88]

In recent decades, yoghurt production has become quite popular due to the enrichment of this type of fermented milk products with various compounds such as vitamins, prebiotics, proteins, omega-3 fatty acids, natural antioxidants [89]. With the advent of the first probiotic-enriched fermented milk product (*Yakult*), and the evaluation of its therapeutic properties, the addition of probiotics or symbiotics is considered quite promising [89,90]. Usually enrichment with probiotics is carried out with the finished product, i.e. before packaging the product or during cooling [90]. Lifophilised cultures of selected probiotics are usually used to enrich yoghurts [87,89].

The yeast *S. boulardii* is microbiota uncharacteristic of fermented milk products. It is known that the strain is used to enrich yoghurt, which contains organic acids, galactose, and glucose [63]. Some studies suggest that there is a symbiotic relationship between yoghurt lactic acid bacteria and *S. boulardii*, in particular, that it can increase riboflavin levels [91] and create favourable conditions for the growth of lactic acid bacteria [63].

Today, there are some studies on the creation of yoghurts containing *S. boulardii*. Since this microorganism actively produces CO_2 (which spoils yoghurt), it is more appropriate to enrich the finished product with a lyophilised or microencapsulated culture [92]. According to the production of drinking yoghurt with the addition of the lyophilised culture of *S. boulardii*, it was found that the survival of all microorganisms was normal, i.e. 10^6 CFU/ml [93], and in the production of yoghurt from goat’s milk, stable survival of *S. boulardii* was also observed [94]. At the same time, microbiological analysis showed a synergistic effect on yeast microorganisms and increased viability throughout the shelf life of the finished product [93]. Studies on the development of symbiotic yoghurt using the microencapsulated probiotic *S. boulardii* and the prebiotic inulin also show good viability of both probiotics and yeast components [95].

Besides the drinking (or fluid) type of yougurt, studies were conducted on frozen yoghurt with both a lyophilised and microencapsulated culture of *S. boulardii* added. It was found that in the product with lyophilised *S. boulardii* added, the survival of the culture is greater than with the microencapsulated culture. The number of lactic acid bacteria was preserved, and the content of yeast cultures was more than 10^6 CFU/ml [92].

Also, there were attempts to create probiotic ice cream using *L. acidophilus* and *S. boulardii.* According to the results, *L. acidophilus* and *S. boulardii*, not individually but in combination, had a significant effect on the intestinal microbiota [96].

Sale prospects of functional fermented milk products enriched with S. boulardii

Dairy products occupy one of the main places in the world's food resources, and demand is at a high level [97]. The modern market of fermented milk products has a wide variety of product names, there are different classifications of dairy products, but yoghurts are the most used and popular. At the same time, the market of functional foods and probiotics is actively developing [98].

According to the statistics from 2013 to 2020 [99] presented and systematised in Fig. 5, there is an increase in demand for yoghurt products. The graphs are based on the code of nomenclature of industrial products (NIP) 10.51.52.45. According to the world reports [99,100], the yoghurt market will grow, with a projected average annual rate of 4.80%.

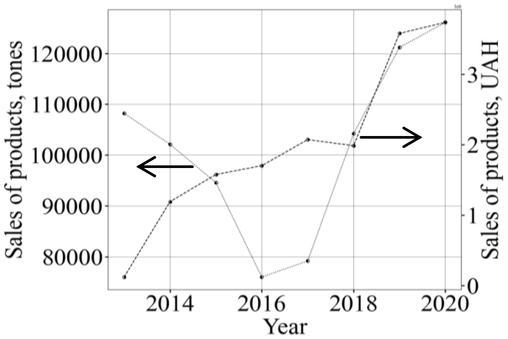

Fig. 5. Statistical information on the sale of yoghurts in UAH, etc., for the period from 2013 to 2020 [99]

The above information proves the obvious feasibility of creating yoghurt in combination with a probiotic strain of *S. boulardii*.

Conclusion

1. Fermented milk products have been known to mankind for a long time, and the history of the technological aspects and research of both fermented milk products and probiotics has been going hand in hand.
2. In the last two decades, there has been an interest in yeast probiotics. *S. boulardii* is one of the first eukariotic probiotics, but it still remains understudied.
3. Certain mechanisms of probiotic action of *S. boulardii* have been established by methods of molecular biology. Today, drugs with *S. boulardii* lyophilisates are considered therapeutically valuable and are actively used in clinical practice.
4. Due to such properties as thermophilicity, resistance to low pH values, and a synergistic effect on other probiotics, it is possible to use *S. boulardii* in combination with other prokaryotic probiotics.
5. One of the prospects of the application of *S. boulardii* is the creation of enriched yoghurt, both drinking and frozen, using lyophilised or microencapsulated cultures.
6. Due to consumers' high demand for and interest in yoghurts and other health-improving products, it is advisable to develop a new probiotic or symbiotic yoghurt.

References:

1. Conto F, editor. Advances in Dairy Products. Chichester, UK: John Wiley & Sons Ltd; 2017. https://doi.org/10.1002/9781118906460
2. Ozen M, Dinleyici EC. The history of probiotics: the untold story. Benef Microbes. 2015 Jan 1;6(2):159-65. https://doi.org/10.3920/BM2014.0103
3. Gasbarrini G, Bonvicini F, Gramenzi A. Probiotics History. J Clin Gastroenterol. 2016 Nov;50(Supplement 2):S116-9. Available from: https://doi.org/10.1097/MCG.0000000000000697
4. Sudhakaran V A, Minj J. Basic Facts About Dairy Processing and Technologies. In: Dairy Processing: Advanced Research to Applications. Singapore: Springer Singapore; 2020. p. 1-24. https://doi.org/10.1007/978-981-15-2608-4_1
5. Trushin M.V. History of research on fermented dairy products. Memoirs of NovSU. 2021 Sep; № 5(38).; 534-537.
6. Lagrange V, Whitsett D, Burris C. Global Market for Dairy Proteins. J Food Sci. 2015 Mar;80(S1):A1622. https://doi.org/10.1111/1750-3841.12801
7. Amiri S, Aghamirzaei M, Mostashari P, Sarbazi M, Tizchang S, Madahi H. The impact of biotechnology on dairy industry. In: Microbial Biotechnology in Food and Health. Elsevier; 2021. p. 53-79. https://doi.org/10.1111/1750-3841.12801
8. Sundarraj AA, Rajathi AA, Vishaal SC, Rohit D, Prakash MS. Food biotechnology applications in dairy and dairy products. J Pharm Res. 2018;12(4):520-5.
9. Pawar S V., Rishi P, editors. Probiotic Research in Therapeutics. Singapore: Springer Singapore; 2021. https://doi.org/10.1007/978-981-33-6236-9
10. Dairy Products Market. Available from: https://www.meticulousresearch.com/product/dairy-products-market-5020.
11. Dairy Products Market Size, Share & Trends Report Dairy Products Market Size, Share & Trends Analysis Report By Product. Available from: https://www.grandviewresearch.com/industry-analysis/dairy-product-market.
12. Fisberg M, Machado R. History of yogurt and current patterns of consumption. Nutr Rev . 2015 Aug 14;73(suppl 1):4-7. https://doi.org/10.1093/nutrit/nuv020
13. Yogurt Market Report 2021. Available from: https://www.globenewswire.com/en/news-release/2021/06/15/2247010/0/en/Yogurt-Market-Report-2021-Market-Size-by-Key-Players-Types-Applications-Countries-Forecast-by-2028.html.
14. Tamime AY, Thomas L V., editors. Probiotic Dairy Products. Chichester, UK: John Wiley & Sons, Ltd; 2017. https://doi.org/10.1002/9781119214137
15. Tamime A. Fermented milks: a historical food with modern applications–a review. Eur J Clin Nutr . 2002 Dec 13;56(S4):S2-15. https://doi.org/10.1038/sj.ejcn.1601657
16. Salque M, Bogucki PI, Pyzel J, Sobkowiak-Tabaka I, Grygiel R, Szmyt M, et al. Earliest evidence for cheese making in the sixth millennium bc in northern Europe. Nature. 2013 Jan 12;493(7433):522-5. https://doi.org/10.1038/nature11698
17. Cramp LJE, Evershed RP, Lavento M, Halinen P, Mannermaa K, Oinonen M, et al. Neolithic dairy farming at the extreme of agriculture in northern Europe. Proc R Soc B Biol Sci. 2014 Sep 22;281(1791):20140819. https://doi.org/10.1098/rspb.2014.0819
18. Jeong C, Wilkin S, Amgalantugs T, Bouwman AS, Taylor WTT, Hagan RW, et al. Bronze Age population dynamics and the rise of dairy pastoralism on the eastern Eurasian steppe. Proc Natl Acad Sci. 2018 Nov 27;115(48):E11248-55. https://doi.org/10.1073/pnas.1813608115
19. Nielsen B, Gürakan GC, Ünlü G. Kefir: A Multifaceted Fermented Dairy Product. Probiotics Antimicrob Proteins . 2014 Dec 27;6(3-4):123-35. https://doi.org/10.1007/s12602-014-9168-0
20. Yu Z, Peng C, Kwok L, Zhang H. The Bacterial Diversity of Spontaneously Fermented Dairy Products Collected in Northeast Asia.

Foods. 2021 Sep 29;10(10):2321. https://doi.org/10.3390/foods10102321
21. Belmer S V. Fermented milk products: from history to the present. Ross Vestn Perinatol i Pediatr (Russian Bull Perinatol Pediatr. 2020 Jan 16;64(6):119–25. https://doi.org/10.21508/1027-4065-2019-64-6-119-125
22. Aryana KJ, Olson DW. A 100-Year Review: Yogurt and other cultured dairy products. J Dairy Sci . 2017 Dec;100(12):9987-10013. https://doi.org/10.3168/jds.2017-12981
23. Tamime AY, Skriver A, Nilsson LE. Starter Cultures. Fermented Milks. 2007;11-52.
24. Durso L, Hutkins R. STARTER CULTURES. In: Encyclopedia of Food Sciences and Nutrition. Elsevier; 2003;5583-93. https://doi.org/10.1016/B0-12-227055-X/01146-9
25. Martins N, Oliveira MBPP, Ferreira ICFR. Development of Functional Dairy Foods. In 2018;1-19. https://doi.org/10.1007/978-3-319-54528-8_35-1
26. Kahn MC. Anaerobic Spore-Bearing Bacteria of the Human Intestine in Health and in Certain Diseases. J Infect Dis. 1924;35(5):423-78.
27. The start of the starter cultures . Available from: https://www.chr-hansen.com/ru/about-us/history#event-the-start-of-the-starter-cultures.
28. Heineman PG. Orla-Jensen's Classification of Lactic Acid Bacteria. J Dairy Sci . 1920 Mar;3(2):143-55. https://doi.org/10.3168/jds.S0022-0302(20)94257-1
29. HISTORY OF DANONE GROUP. Available from: https://danone.ua/en/about-company/history/?no_cache=1.
30. Rettger LF, Cheplin HA. Therapeutic application of Bacillus acidophilus. Exp Biol Med. 1921 Nov 1;19(2):72-6. https://doi.org/10.3181/00379727-19-38
31. Lactobacillus Acidophilus and Its Therapeutic Application. J Am Med Assoc. 1936 Feb 22;106(8):648. http://doi:10.1001/jama.1936.02770080062030
32. The same profile since 1935 . Available from: https://yakult.com.mt/since-1935/.
33. Pette JW, Lolkema H. Yoghurt. 1. Symbiosis and antibiosis in mixed cultures of Lactobacillus bulgaricus and Streptococcus thermophilus. Ned Melk- en Zuiveltijdschr. 1950;4:197-208.
34. Reddy G V., Shahani KM, Banerjee MR. Inhibitory Effect of Yogurt on Ehrlich Ascites Tumor-Cell Proliferation. JNCI J Natl Cancer Inst. 1973;50(3):815-817.
35. Mann G V., Spoerry A. Studies of a surfactant and cholesteremia in the Maasai. Am J Clin Nutr. 1974 May 1;27(5):464-9. https://doi.org/10.1093/ajcn/27.5.464
36. Terzaghi BE, Sandine WE. Improved Medium for Lactic Streptococci and Their Bacteriophages. Appl Microbiol . 1975 Jun;29(6):807-13. https://doi.org/10.1128/am.29.6.807-813.1975
37. Kalab M, Emmons DB, Sargant AG. Milk-gel structure. IV. Microstructure of yoghurts in relation to the presence of thickening agents. J Dairy Res. 1975 Oct 1;42(3):453–8. https://doi.org/10.1017/S0022029900015491
38. Porch K. Lactose-Free Milk, Low-Fat Cheese, and More Dairy Breakthroughs. 2018. Available from: https://federallabs.org/successes/success-stories/lactose-free-milk-low-fat-cheese-and-more-dairy-breakthroughs
39. Robinson RK. The potential of inulin as a functional ingredient. Br Food J . 1995 May;97(4):30–2. https://doi.org/10.1108/00070709510085657 l
40. Anbukkarasi K, UmaMaheswari T, Hemalatha T, Nanda DK, Singh P, Singh R. Preparation of low galactose yogurt using cultures of Gal+ Streptococcus thermophilus in combination with Lactobacillus delbrueckii ssp. bulgaricus. J Food Sci Technol . 2014 Sep 2;51(9):2183-9. https://doi.org/10.1007/s13197-014-1262-5
41. Abdizhanova Zh. A. The history of the creation of a new generation of functional dairy products with prebiotic microorganisms. In: Food innovation and biotechnology. Volume 1. Biotechnology, quality and safety ; 2020 May 25-27; Kemerovo, Russia. Kemerovo State University; 2020 [cited 2021 Nov 17]; p. 340. Available from: https://elibrary.ru/download/elibrary_42944550_63379495.pdf
42. Vankar KD. Dairy Engineering: A Keystone to the Dairy Industry. In: Dairy Processing: Advanced Research to Applications . Singapore: Springer Singapore; 2020. p. 51-61. https://doi.org/10.1007/978-981-15-2608-4_3
43. Bhat ZF, Bhat H. Milk and Dairy Products as Functional Foods: A Review. Int J Dairy Sci . 2010 Dec 15;6(1):1–12. https://doi.org/10.3923/ijds.2011.1.12
44. Topolska K, Florkiewicz A, Filipiak-Florkiewicz A. Functional Food – Consumer Motivations and Expectations. Int J Environ Res Public Health. 2021 May 17;18(10):5327. https://doi.org/10.3390/ijerph18105327
45. Granato D, Barba FJ, Bursać Kovačević D, Lorenzo JM, Cruz AG, Putnik P. Functional Foods: Product Development, Technological Trends, Efficacy Testing, and Safety. Annu Rev Food Sci Technol. 2020 Mar 25;11(1):93-118. https://doi.org/10.1146/annurev-food-032519-051708
46. Panesar PS. Fermented Dairy Products: Starter Cultures and Potential Nutritional Benefits. Food Nutr Sci . 2011;02(01):47-51. https://doi.org/10.4236/fns.2011.21006
47. Gibson M, Newsham P. Milk and Dairy. In: Food Science and the Culinary Arts. Elsevier. 2018;133-67. https://doi.org/10.1016/B978-0-12-811816-0.00011-7
48. Meunier-Goddik L. Sour Cream and Crème Fraîche. In: Handbook of Animal-Based Fermented Food and Beverage Technology. CRC Press; 2012; 235-46. https://doi.org/10.1201/b12084-16
49. Kopanos GM, Puigjaner L, Georgiadis MC. Optimal Production Scheduling and Lot-sizing In Yoghurt Production Lines. In: Industrial & Engineering Chemistry Research. 2010;1153-8. https://doi.org/10.1016/S1570-7946(10)28193-2
50. Derzhspozhyvstandart of Ukraine. DSTU 4343: 2004
51. Khalighi A, Behdani R, Kouhestani S. Probiotics: A Comprehensive Review of Their Classification, Mode of Action and Role in Human Nutrition. In: Probiotics and Prebiotics in Human Nutrition and Health. InTech; 2016. https://doi.org/10.5772/63646
52. Gómez-Gallego C, Gueimonde M, Salminen S. The role of yogurt in food-based dietary guidelines. Nutr Rev . 2018 Dec 1;76(Supplement_1):29-39. https://doi.org/10.1093/nutrit/nuy059
53. de Vrese M, Schrezenmeir J. Probiotics, Prebiotics, and Synbiotics. 2008;1-66. https://doi.org/10.1007/10_2008_097
54. Ortiz Y, García-Amézquita E, Acosta CH, Sepúlveda DR. Functional Dairy Products. In: Global Food Security and Wellness . New York, NY: Springer New York. 2017;67-103. https://doi.org/10.1007/978-1-4939-6496-3_5
55. Zheng J, Wittouck S, Salvetti E, Franz CMAP, Harris HMB, Mattarelli P, et al. A taxonomic note on the genus Lactobacillus: Description of 23 novel genera, emended description of the genus Lactobacillus Beijerinck 1901, and union of Lactobacillaceae and Leuconostocaceae. Int J Syst Evol Microbiol. 2020 Apr 1;70(4):2782-858. https://doi.org/10.1099/ijsem.0.004107
56. Büchl NR, Seiler H. Yeasts and Molds: Yeasts in Milk and Dairy Products. Encycl Dairy Sci Second Ed. 2011;744-53.
57. Liong M-T, editor. Probiotics. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011. (Microbiology Monographs; vol. 21). https://doi.org/10.1007/978-3-642-20838-6
58. Kumura H, Tanoue Y, Tsukahara M, Tanaka T, Shimazaki K. Screening of Dairy Yeast Strains for Probiotic Applications. J Dairy Sci. 2004 Dec;87(12):4050-6. https://doi.org/10.3168/jds.S0022-0302(04)73546-8
59. Ansari F, Alian Samakkhah S, Bahadori A, Jafari SM, Ziaee M, Khodayari MT, et al. Health-promoting properties of Saccharomyces

cerevisiae var. boulardii as a probiotic; characteristics, isolation, and applications in dairy products. Crit Rev Food Sci Nutr. 2021 Jul 13;1-29. https://doi.org/10.1080/10408398.2021.1949577

60. Malaviya A, Malviya S, Agarwal A, Mishra M, Dalmida V. Saccharomyces - Eukaryotic Probiotic for Human Applications. In: High Value Fermentation Products. Hoboken, NJ, USA: John Wiley & Sons, Inc. 2019; 211-29. https://doi.org/10.1002/9781119555384.ch11
61. Khatri I, Tomar R, Ganesan K, Prasad GS, Subramanian S. Complete genome sequence and comparative genomics of the probiotic yeast Saccharomyces boulardii. Sci Rep. 2017; Dec 23;7(1):371. https://doi.org/10.1038/s41598-017-00414-2
62. Ukaszewicz M. Saccharomyces cerevisiae var. boulardii – Probiotic Yeast. In: Probiotics. InTech; 2012. http://dx.doi.org/10.5772/50105
63. Lazo-Vélez MA, Serna-Saldívar SO, Rosales-Medina MF, Tinoco-Alvear M, Briones-García M. Application of Saccharomyces cerevisiae var. boulardii in food processing: a review. J Appl Microbiol. 2018 Oct;125(4):943-51. https://doi.org/10.1111/jam.14037
64. McFarland LV. Saccharomyces boulardii Is Not Saccharomyces cerevisiae. Clin Infect Dis. 1996;Jan 1;22(1):200-1. https://doi.org/10.1093/clinids/22.1.200
65. Pais P, Almeida V, Yılmaz M, Teixeira MC. Saccharomyces boulardii: What Makes It Tick as Successful Probiotic? J Fungi. 2020; Jun 4;6(2):78. https://doi.org/10.3390/jof6020078
66. Mitterdorfer G, Kneifel W, Viernstein H. Utilization of prebiotic carbohydrates by yeasts of therapeutic relevance. Lett Appl Microbiol. 2001 Oct 17;33(4):251–5. https://doi.org/10.1046/j.1472-765X.2001.00991.x
67. Edwards-Ingram L, Gitsham P, Burton N, Warhurst G, Clarke I, Hoyle D, et al. Genotypic and Physiological Characterization of Saccharomyces boulardii , the Probiotic Strain of Saccharomyces cerevisiae. Appl Environ Microbiol. 2007 Apr 15;73(8):2458-67. ttps://doi.org/10.1128/AEM.02201-06
68. Khatri I, Akhtar A, Kaur K, Tomar R, Prasad GS, Ramya TNC, et al. Gleaning evolutionary insights from the genome sequence of a probiotic yeast Saccharomyces boulardii. Gut Pathog. 2013 Dec 22;5(1):30. https://doi.org/10.1186/1757-4749-5-30
69. Saccharomyces boulardii (nom. inval.). Available from: https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?mode=Info&id=252598&lvl=3&keep=1&srchmode=1&unlock&lin=s&log_op=lineage_toggle.
70. Pais P, Oliveira J, Almeida V, Yilmaz M, Monteiro PT, Teixeira MC. Transcriptome-wide differences between Saccharomyces cerevisiae and Saccharomyces cerevisiae var. boulardii: Clues on host survival and probiotic activity based on promoter sequence variability. Genomics. 2021 Mar; 113(2):530-9. https://doi.org/10.1016/j.ygeno.2020.11.034
71. Tomicic Z, Colovic R, Cabarkapa I, Vukmirovic D, Djuragic O, Tomicic R. Beneficial properties of probiotic yeast Saccharomyces boulardii. Food Feed Res. 2016;43(2):103-10. https://doi.org/10.5937/FFR1602103T
72. Srinivas B, Rani GS, Kumar BK, Chandrasekhar B, Krishna KV, Devi TA, et al. Evaluating the probiotic and therapeutic potentials of Saccharomyces cerevisiae strain (OBS2) isolated from fermented nectar of toddy palm. AMB Express. 2017 Dec 3;7(1):2. https://doi.org/10.1186/s13568-016-0301-1
73. Fernandez-Pacheco P, Arévalo-Villena M, Bevilacqua A, Corbo MR, Briones Pérez A. Probiotic characteristics in Saccharomyces cerevisiae strains: Properties for application in food industries. LWT. 2018 Nov;97:332-40. https://doi.org/10.1016/j.lwt.2018.07.007
74. Kaźmierczak-Siedlecka K, Ruszkowski J, Fic M, Folwarski M, Makarewicz W. Saccharomyces boulardii CNCM I-745: A Non-bacterial Microorganism Used as Probiotic Agent in Supporting Treatment of Selected Diseases. Curr Microbiol. 2020 Sep 29;77(9):1987-96. https://doi.org/10.1007/s00284-020-02053-9
75. Lawson PA, Citron DM, Tyrrell KL, Finegold SM. Reclassification of Clostridium difficile as Clostridioides difficile (Hall and O'Toole 1935) Prévot 1938. Anaerobe. 2016 Aug; 40:95–9. https://doi.org/10.1016/j.anaerobe.2016.06.008
76. Kunyeit L, Kurrey NK, Anu-Appaiah KA, Rao RP. Probiotic Yeasts Inhibit Virulence of Non -albicans Candida Species. Heitman J, editor. MBio. 2019 Oct 29;10(5). https://doi.org/10.1128/mBio.02307-19
77. Namkin K, Zardast M, Basirinejad F. Saccharomyces Boulardii in Helicobacter Pylori Eradication in Children: A Randomized Trial From Iran. Iran J Pediatr. 2016 Jan 30;26(1). https://doi.org/10.5812/ijp.3768
78. Akhondi-Meybodi M, Rahimian M, Salmanroghani H, Amirbeigy M, Baghbanian M, Ghelmani S. Study of the Effect of Probiotic Saccharomyces Boulardii on the Treatment of Irritable Bowel Syndrome. J Biol Today's World. 2014;3(7). http://doi:10.15412/J.JBTW.01030703
79. Szajewska H, Kołodziej M, Zalewski BM. Systematic review with meta-analysis: Saccharomyces boulardii for treating acute gastroenteritis in children-a 2020 update. Aliment Pharmacol Ther. 2020 Apr;51(7):678-88. https://doi.org/10.1111/apt.15659
80. Moens F, Duysburgh C, van den Abbeele P, Morera M, Marzorati M. Lactobacillus rhamnosus GG and Saccharomyces cerevisiae boulardii exert synergistic antipathogenic activity in vitro against enterotoxigenic Escherichia coli. Benef Microbes. 2019 Dec 9;10(8):923-35. https://doi.org/10.3920/BM2019.0064
81. McFarland L V. Systematic review and meta-analysis of Saccharomyces boulardii in adult patients. World J Gastroenterol. 2010;16(18):2202. https://doi.org/10.3748/wjg.v16.i18.2202
82. Moré MI, Vandenplas Y. Saccharomyces boulardii CNCM I-745 Improves Intestinal Enzyme Function: A Trophic Effects Review. Clin Med Insights Gastroenterol. 2018 Jan 1;11:117955221775267. https://doi.org/10.1177/1179552217752679
83. Palma ML, Zamith-Miranda D, Martins FS, Bozza FA, Nimrichter L, Montero-Lomeli M, et al. Probiotic Saccharomyces cerevisiae strains as biotherapeutic tools: is there room for improvement? Appl Microbiol Biotechnol. 2015 Aug 4;99(16):6563-70. https://doi.org/10.1007/s00253-015-6776-x
84. Sulik-Tyszka B, Snarski E, Niedźwiedzka M, Augustyniak M, Myhre TN, Kacprzyk A, et al. Experience with Saccharomyces boulardii Probiotic in Oncohaematological Patients. Probiotics Antimicrob Proteins. 2018 Jun 25;10(2):350-5. https://doi.org/10.1007/s12602-017-9332-4
85. Dinleyici EC, Eren M, Ozen M, Yargic ZA, Vandenplas Y. Effectiveness and safety of Saccharomyces boulardii for acute infectious diarrhea. Expert Opin Biol Ther. 2012 Apr 16;12(4):395-410. tps://doi.org/10.1517/14712598.2012.664129
86. Ürkek B, Sengül M, Erkaya T. Use of Saccharomyces boulardii in Fermented Dairy Products. 2014;12(2):108–13.
87. Sfakianakis P, Tzia C. Dairy technologies in yogurt production. In: Microbiology in Dairy Processing. Chichester, UK: John Wiley & Sons Ltd and the Institute of Food Technologists; 2017; 279-98. https://doi.org/10.1002/9781119115007.ch15
88. Hand M, Hand M, Some P, Hand M, Hand M, Ions A, et al. Dairy Processing Handbook.
89. Minj J, Dogra S. Significance of Fortification of Beneficial Natural Ingredients in Milk and Milk Products. In: Dairy Processing: Advanced Research to Applications. Singapore: Springer Singapore; 2020. p. 87-118. https://doi.org/10.1007/978-981-15-2608-4_5
90. Hashemi Gahruie H, Eskandari MH, Mesbahi G, Hanifpour MA. Scientific and technical aspects of yogurt fortification: A review. Food Sci Hum Wellness. 2015 Mar;4(1):1-8. https://doi.org/10.1016/j.fshw.2015.03.002
91. Chandrasekar Rajendran SC, Chamlagain B, Kariluoto S, Piironen V, Saris PEJ. Biofortification of riboflavin and folate in idli batter, based on fermented cereal and pulse, by Lactococcus lactis N8 and Saccharomyces boulardii SAA655. J Appl Microbiol. 2017 Jun;122(6):1663-71. https://doi.org/10.1111/jam.13453
92. Martinez-Flores HE, Tranquilino-Rodriguez E, Rodiles-Lopez JO, Zamora-Vega R, Salgado-Garciglia R, Perez-Sanchez RE. Survival rate

of Saccharomyces boulardii adapted to a functional freeze-dried yoghurt, related to processing, storage and digestion by experimental Wistar rats. Funct Foods Heal Dis. 2017 Mar 1;7(2):98. https://doi.org/10.31989/ffhd.v7i2.319

93. Niamah A. Physicochemical and Microbial Characteristics of Yogurt with Added Saccharomyces Boulardii. Curr Res Nutr Food Sci J . 2017 Dec 24;5(3):300-7. https://dx.doi.org/10.12944/CRNFSJ.5.3.15
94. Karaolis C, Botsaris G, Pantelides I, Tsaltas D. Potential application of Saccharomyces boulardii as a probiotic in goat's yoghurt: survival and organoleptic effects. Int J Food Sci Technol. 2013 Jul;48(7):1445-52. https://doi.org/10.1111/ijfs.12111
95. Sarwar A, Aziz T, Al-Dalali S, Zhao X, Zhang J, ud Din J, et al. Physicochemical and Microbiological Properties of Synbiotic Yogurt Made with Probiotic Yeast Saccharomyces boulardii in Combination with Inulin. Foods. 2019 Oct 10;8(10):468. https://doi.org/10.3390/foods8100468
96. Pandiyan C, Annal Villi R, Kumaresan G, Murugan B, Gopalakrishnamurthy TR. Development of synbiotic ice cream incorporating lactobacillus acidophilus and saccharomyces boulardii. Int Food Res J. 2012;19(3):1233-9.
97. Velichko A, Kuharuk R, Maslova I, Pukhlyakova M. STATE AND PROSPECTS OF DEVELOPMENT OF THE MARKET OF MILK AND DAIRY PRODUCTS OF UKRAINE. Agrosvit. 2021 Aug 31;(16):62. Available from: http://www.agrosvit.info/?op=1&z=3480&i=7
98. Clydesdale F. Opportunities and challenges for developing functional foods. Genet Eng News. 2005;25(9).
99. Sales of industrial products by type. Available from: http://www.ukrstat.gov.ua/.
100. Global Yogurt Market – Industry Trends and Forecast to 2028. Available from: https://www.databridgemarketresearch.com/reports/global-yogurt-market.

ПОТЕНЦІАЛ ВИКОРИСТАННЯ *SACCHAROMYCES BOULARDII* У ВИРОБНИЦТВІ КИСЛОМОЛОЧНИХ ПРОДУКТІВ

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Анотація. Проведений аналіз літератури дозволяє охарактеризувати потенціал використання нового пробіотичного штаму дріжджів *S. boulardii*. Стаття описує тривалий період становлення фундаментальних знань та впровадження технологічних прийомів у виробництві різних кисломолочних продуктів. Окрім історичного аспекту, розглядається мікробіологічна різноманітність кисломолочних продуктів та відмінності технологій їх виробництва. Відомо, що одним із найвідоміших кисломолочних продуктів є йогурт. Цей кисломолочний продукт роками користується великою популярністю через свої смакові характеристики та простоту виготовлення. З накопиченням знань щодо пробіотиків та технології виробництва йогуртів з'явилась тенденція до додаткового збагачення продукту певними пробіотиками, пробіотиками та мінералами. Сьогодні у виробництві йогуртів активно використовується методика збагачення готового продукту пробіотиками, що дозволяє створити якісно новий функціональний продукт харчування, що має не тільки харчову цінність для споживача, але і певний позитивний вплив на мікробом кишківника, а отже і на здоров'я споживача. Відомо, що основними пробіотиками є бактерії, однак нещодавнє відкриття пробіотичних властивостей певних родів та видів дріжджів відкриває нові перспективи їх використання, як у фармацевтичній галузі, так і для створення функціональних продуктів харчування. Нещодавно відкритий штам дріжджів *S. boulardii,* філогенетично споріднений з *S. cerevisiae,* має безліч терапевтичних ефектів та значні переваги перед бактеріальними пробіотиками, зокрема, стійкість до антибіотиків. Саме *S. boulardii* є пробіотичним штамом, що може бути використаний для збагачення йогурту. Фізіологічні властивості штаму та терапевтичні властивості продуктів метаболізму, у поєднані з розглянутими технологічними параметрами виробництва йогуртів, дають перспективу комбінації цього пробіотика та корисного питного кисломолочного продукту. Визначено, що для виробництва збагаченого йогурту можливе використання як ліофілізованої культури *S. boulardii*, так і мікроінкапсульованої. Проаналізувавши економічний аспект, а саме реалізацію йогуртів та подальшу тенденцію до росту споживання, можна сказати, що впровадження *S. boulardii,* як штаму для збагачення йогурту, є досить актуальним та перспективним.

Ключові слова: дріжджі, йогурт, пробіотики, біотехнологія, функціональні продукти харчування, харчові технології.