# **Systematic review**

## Biological value of yak milk and its importance in medical and functional nutrition: A systematic review

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## Abstract

**Objective:** Yak milk is a unique product with a high content of proteins, essential amino acids, fatty acids, vitamins and minerals. It is traditionally used in the diet of the population of the mountainous regions of Central Asia, especially in Kyrgyzstan, and has significant potential as a functional and dietary product. Due to its composition, yak milk can help strengthen the immune system, improve metabolism and prevent chronic diseases. Despite its value, the chemical composition and biological properties of yak milk remain poorly understood, especially in comparison with other types of milk.

The purpose of this review article is to systematize and summarize current scientific data on the chemical composition of yak milk, analyze its potential medicinal and functional properties, and assess the prospects for using this product in medical practice and functional nutrition.

**Methods:** An analytical review of the scientific literature devoted to the study of the chemical composition of yak milk and its therapeutic and functional properties was conducted. Data from Google Scholar, Scopus, Web of Science and other scientific databases were used.

**Results:** During the literature review, 428 articles were analyzed, of which 88 were included in the final review. A review of the available modern information reveals the potential of yak milk as a source of nutrients and functional substances. The article presents the results of scientific studies of the chemical composition of yak milk and analyzes the data provided depending on the habitat of yaks. Yak milk has a high content of protein and essential amino acids, fat and fatty acids, vitamins and minerals. Scientific studies have shown that yak milk and its bioactive components have antioxidant, anticancer, antibacterial, antihypertensive, anti-inflammatory, hypocholesterolemic, antihypoxic, immunomodulatory, antidiabetic, tonic, and laxative properties. These properties provide prospects for the development of functional products with the addition of yak milk.

**Conclusion:** Yak milk has a unique composition rich in nutrients and bioactive components, which gives it significant medicinal and functional properties. This opens up prospects for its use in medicine, dietary nutrition, and the creation of preventive agents.

Key words: Yak milk, proteins, amino acids, fats, fatty acids, minerals, vitamins, medicinal and functional properties. (Heart Vessels Transplant 2025; 9: doi: 10.24969/hvt.2025.575)

## Introduction

Dairy products from the milk of the yak are popular products in the highland regions of China, Mongolia, southern Russia and Central Asian countries, they are one of the main components in the diet of shepherds who spend most of their lives on high-mountain pastures. They are especially useful for a weakened and elderly body, due to their biochemical composition.

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The purpose of this analytical review article is to summarize modern data obtained from scientific databases (such as Google Scholar, Scopus, Web of Science and others) on the biological value of yak milk, its medicinal and functional properties, and to study the prospects for its use in medicine.



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The study of the milk of the yak living on the highmountain pastures of Kyrgyzstan is of interest because at the moment there is little information about its composition and functional effect on the human body. Kyrgyzstan is a country of vast high-mountain pastures with a unique combination of natural and climatic conditions for grazing yaks.

Yaks are well adapted to the specific conditions of the highlands, characterized by low partial pressure and air temperature, with low and sparse flora. In Kyrgyzstan, they are usually bred at an altitude of over 2500 m above sea level.

The experience of yak breeders shows that in Kyrgyzstan, yaks can be kept in winter in areas with an altitude of

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1800-2000 m above sea level, but in summer, keeping them at such an altitude becomes impossible. With the onset of spring, they must be driven high into the mountains, and the higher the air temperature in a given area, the higher the pastures should be above sea level (2800-3000 m).

The purpose of this review article is to systematize and summarize current scientific data on the chemical composition of yak milk, analyze its potential medicinal and functional properties, and assess the prospects for using this product in medical practice and functional nutrition.

## Methods

To write the review, a systematic search of scientific literature was conducted, covering publications over the past 15 years (2009-2024). The main sources of information were international and domestic scientific databases: PubMed, Scopus, Web of Science, Google Scholar, eLIBRARY, and CyberLeninka. The search was carried out using key words and phrases in both English and Russian, including: "vak milk composition", "bioactive components of yak milk", "yak milk health benefits", "functional foods from yak milk", "yak milk medicinal properties", "yak milk", "medicinal properties of milk", "functional nutrition", and other relevant terms. The logical operators AND/OR were used, as well as filters by publication date and language. The review included peerreviewed scientific articles, original studies, analytical works and scientific reviews containing information on the chemical composition of yak milk, its nutritional value, biologically active components and

potential therapeutic effects. Publications that had not undergone scientific peer review, duplicate studies, as well as sources that were not relevant to the topic of the work (e.g. articles devoted to yak meat or wool) were excluded. The selection and analysis of literature were carried out manually in two stages: first, based on titles and abstracts, then on the full text of publications. The selected sources were critically assessed, taking into account such parameters as scientific validity, reliability of the data presented and transparency of the methodology. Information from the included works was systematized, analyzed and grouped into main thematic areas: the chemical composition of yak milk, its biological activity, functional and therapeutic properties. All results were structured in accordance with the purpose of the study.

The process of literature selection is presented in the diagram (see Figure 1).



### Figure 1. Scheme for selecting publications for inclusion in the review

## Composition of yak milk

The nutritional and biological values of milk, as well as its technological properties, are determined by the biochemical composition, which depends on a number of factors, including the season of the year, the breed of the animal, its physiological condition, age, region of habitat, etc.

Yak milk has medicinal and functional properties, since yaks, being exclusively pasture animals, have the ability to process finely dispersed energy of plants growing at high altitudes (1, 2).

Milk is a complex colloidal dispersion containing fat globules, casein micelles and whey proteins in an aqueous solution of lactose, minerals and some other minor compounds. Yak milk contains on average 16.9–

17.7% dry matter, 4.9–5.3% protein, 5.5–7.2% fat, 4.5–5.0% lactose and 0.8–0.9% minerals (3-5).

Due to the poor availability of the studied material, yak milk has not been well studied, however, there are research results from some scientists in Tuva, Altai, China and Kyrgyzstan, which provide characteristics of the chemical composition of female yak milk (Table 1) (5-7).

The milk of the Altai yak breed has the highest fat content, and the milk of the yak breed that lives in Kyrgyzstan has the highest protein and lactose content. The milk of the Khainachka breed is inferior in protein and lactose content to the milk of the yak breed, but hybrid yak breeds are distinguished by better milk productivity and a higher fat content than ordinary yak breeds (8).

Biochemical		Milk			
indicators	Yak,	Yak, Yak,		Hainak* (yak hybrid),	
	Kyrgyzstan (6)	China (5)	Altai (7)	Kyrgyzstan (8)	
Fat, %	5.4	6.1	7.7	5.58	
Protein, %	5.66	4.95	5.3	4.29	
Lactose, %	5.6	5.5	5.1	4.84	

Note\* Hainak or hainyk is a hybrid of a yak and a cow, a hainachka is a female hainak. Hybridization of yak and cattle occurs naturally and artificially. Hybrids of cattle and yak are as resistant to high altitudes as purebred yaks, but have a high milk yield.

## Proteins in yak milk

In yak milk, as in any milk of ruminants, the main protein is casein, which accounts for more than 60% of all proteins present. The ratio of casein to whey protein varies depending on the type of mammal (9, 10).

Yak milk has a higher protein content (46.2–58.4 g/l), including casein of about 40.2 g/l. The high content of  $\beta$ -

casein (more than 45%) and, accordingly, the low proportion of  $\alpha$ s-casein (about 40%), the rest being k-casein (15%), make yak milk suitable for baby food (11-15).

The whey protein content is higher in the milk of Kyrgyz yachikha (Table 2).

Indicators	Yak milk, Kyrgyzstan	Yak milk, China	Hainak, Kyrgyzstan	Cow milk, (13)
Whey protein content, %	1.57 (0.75)	1.1	1.01 0.08)	0.82(0.05)
α-Lactalbumin (α-LA), mg/cm3	1.58 (0.09)	0.72	2.120 (0.103)	1.24
β-Lactoglobulin A (β-LG A), mg/cm3	0.661 (0.12)	0.74	0.790 (0.090)	3.30
β-Lactoglobulin B (β-LG B)	1.32 (0.05)	5.49	1.560 (0.110)	
Content of casein proteins, %	3.32 (0.75)	2.1 - 4.0	3.02 (0.40)	2.57
Total nitrogen content, %	0.773 (0.16)	0.79 (0.04)	0.66 (0.03)	0.528 (0.006)
Non-protein nitrogen content, %	0.03485 (0.00007)	0.04 (0.01)	0.0425 (0.0008)	0.0320 (0.0030)

Table 2. Protein composition of yak milk of the Kyrgyz and Chinese populations, hainak (hybrid) and cow

Whey protein is a good source of essential amino acids. There is more  $\alpha$ -Lactalbumin ( $\alpha$ -LA) of whey proteins in the milk of Kyrgyz yachikha than in the milk of Chinese yachikha, but it is inferior in the content of  $\beta$ -Lactoglobulin.  $\alpha$ -LA is the second main whey protein, it is involved in the synthesis of lactose and promotes milk secretion. When it is digested, peptides with antibacterial and immunostimulating properties are formed, which helps protect against infection. Therefore, it is recommended to add it to baby formulas

to increase its biological value. In addition,  $\beta$ lactoglobulin dominates in the overall aggregation and gelation of whey protein preparations (16, 17). The ratio of  $\beta$ -LG A and ( $\beta$ -LG B) is influenced by the genotypes of milk protein, stage of lactation, season, feeding, etc. ((16, 17).

#### Amino acid composition of yak milk protein

The nutritional value of proteins is determined by the qualitative and quantitative ratio of individual amino acids (4).

Amino acids, mg/100g	Milk				
	Yak milk,	Yak milk,	Hainak, Kyrgyzstan	Cow	
	Kyrgyzstan	China			
Essential amino acids	2785.23	1950	1824	1380	
Threonine	290.65	190	180	150	
Valin	311.7	260	223	160	
Methionine	188.1	110	108	60	
Lysine	529.7	380	360	270	
Phenylalanine	323.8	220	247	160	
Histidine	178.15	120	143	100	
Leucine-isoleucine	927.45	670	540	430	
Tryptophan	35.68	-	23	50	
Replaceable amino acids	3065.58	2750	2168	1950	
Arginine	236.95	160	155	110	
Serin	326.15	230	253	160	
Alanin	269.7	140	186	100	
Proline	796.5	460	470	320	
Glycine	117.0	120	97	60	
Tyrosine	320.85	220	215	150	
Aspartic acid	313.0	330	253	260	
Cysteine	33.38	40	31	20	
Glutamic acid	652.05	1050	507	770	
Total amino acid content	5850.81	4700	3992	3330	
Ratio: essential/non-essential, %	91	71	84	71	
Ratio: essential/total content, %	47	41	45	41	

Yak milk contains more amino acids than hainak and cow milk, which is due to the high content of total milk protein. High protein content in milk is important for the prevention of deficiency of complete proteins, which is important for healthy human nutrition. Lack of protein in the diet contributes to a decrease in the body's resistance to various infectious diseases, adversely affects the functions of human systems. Protein amino acids are the material for the growth and restoration of muscle mass, so milk and products from it can be recommended for pregnant women, children, athletes and people with cardiovascular (CV) diseases. The ratio of replaceable and essential amino acids in the milk of Kyrgyz yaki is 91%, and the ratio of essential to the total amino acid content is 47%, these

are the highest figures among the given values, and they fully comply with the recommended FAO / WHO values, which are 60% and 40%, respectively (18). Fat content in yak milk

Due to the unique flora of high-mountain pastures, the fat phase of yak milk is unique in its fatty acid (FA) composition compared to the corresponding composition of other mammals (18, 19).

Dairy FAs have a significant impact on human health. Saturated fatty acids (SFA) consumed with milk and dairy products have a negative impact on the human body and cause certain health problems. It is believed that high consumption of especially short- and medium-chain SFAs increases the risk of developing CV diseases. Yak milk fat is rich in polyunsaturated fatty acids (PUFA) and conjugated linoleic acid (CLA) (20, 21). The

comparative composition of milk of Kyrgyz (22) and Chinese yak breeds (3) is given in Table 5.

Table 5. Composition of fatty acids in yak and cow milk					
Fatty acid, %	Yachikha milk,	Yachikha milk,	Cow's milk,		
	Kyrgyzstan <mark>(22)</mark>	China (3)	Russia <mark>(24)</mark>		
Caproic C6:0	1.74	1.49	1.81		
Capric C8:0	0.75	0.92	1.13		
Capric C10:0	1.5	1.75	2.55		
Lauric C12:0	1.8	1.47	2.98		
Myristic C14:0	10.1	6.25	10.16		
Palmitic C16:0	33.6	22.06	29.0		
Stearic C18:0	8.2	15.03	11.04		
Arachidic C20:0	0.5	0.69	0.21		
Beghenic C22:0	0.1	0.35	0.08		
Myristoleic C14:1	0.7	0.29	0.86		
Palmitoleic C16:1	2.4	0.27	1.73		
Oleic C18:1	29.7	31.81	26.32		
Linoleic C18:2	1.6	0.76	3.23		
Conjugated linoleic (C18:2, cis-9)	1.7	2.57	0.5-0.6		
Linolenic C18:3	0.77	2.7	0.6		

The presence of unsaturated, essential fatty acids such as linoleic and arachidonic acids in milk fat plays an important role, as they are necessary for the human body. PUFAs are necessary for the proper development of a young organism, as well as maintaining a person's well-being. These acids belong to the  $\omega$ -6 and  $\omega$ -3 family (23). Scientific studies have proven that omega-3 fatty acids are required for normal brain function, since they quickly provide the energy needed to transmit a signal from cell to cell (24). CLA is believed to have some anti-carcinogenic properties, as well as a number of positive effects on human health, including a beneficial effect on reducing the amount of fat in the body, reducing the development of type 2 diabetes, slowing the development of atherosclerosis, improving bone mineralization and modulating the immune system. Monounsaturated and long-chain polyunsaturated fatty acids (MUFA and LC-PUFA) play a very important role in some biological processes in the human body. The fat phase of yak milk has the highest concentration of MUFA. Oleic acid is the most

concentration of MUFA. Oleic acid is the most common MUFA in the milk of ruminants. In yak milk, it accounts for 19.53–22.81% of the MUFA (25, 26). Oleic acid prevents diabetes and has antioxidant properties (26). The fat phase of yak milk also has a high content of conjugated linoleic acid, which is one of the important functional fatty acids (27).

### Minerals

In general, the mineral content of yak milk has not been sufficiently studied at the moment, although this data could be of significant nutritional and medical interest.

The most important minerals are calcium, sodium, potassium and magnesium. At the same time, calcium and phosphorus in milk are in an easily digestible form and well-balanced ratios and are necessary in the processes of bone formation and hematopoiesis (20). This is especially important for the child's body, in which bone tissue formation occurs very intensively.

From Table 6 it is clear that the mineral content in yak milk from different regions of habitat significantly exceeds the mineral content in cow's milk.

Yak milk is richer in mineral content than cow's milk, especially in such minerals as calcium, zinc, selenium and silicon (Table 6). The spectrum and quantitative content of individual trace elements in milk is determined by the biogeochemical characteristics of the region (28, 29).

Table 6. Comparative review of the mineral composition of milk of female yaks living in different     regions (29, 30) and cow's milk					
Minerals, µg/g	Yak milk, China	Yak milk, Kyrgyzstan	Cow milk		
Calcium	803.0 (124.0)	934.8 (38.9)	516.0 (78.0)		
Magnesium	96.7 (12.3)	129.5 (3.5)	83.2 (10.3)		
Sodium	345.0 (59.0)	636.9 (19.21)	292.0 (50.0)		
Potassium	1363.0 (200.0)	1416.5 (18.08)	1242.0 (279.0)		
Iron	2.54 (0.64)	1.02 (0.59.0)	1.45 (0.52)		
Copper	0.522 (0.115)	0.15 (0.085)	0.165 (0.058)		
Manganese	0.256 (0.061)	0.00074 (0.00015)	0.0187 (0.125)		
Zinc	4.76 (1.0-49.0)	7.93 (1.96)	4.36 (1.27)		

The milk of the Kyrgyz yak contains, on average, more minerals than the milk of the Chinese yak and cow. It is second only in iron, manganese and copper (30).

#### Vitamins

Vitamins A, E and C are the main antioxidants and help eliminate free radicals. Vitamin A also plays an important role in maintaining good vision. Extensive research shows that increasing the intake of antioxidant vitamins, especially vitamin E, is useful in reducing oxidative stress in the human body, especially caused by high altitude.

Research on Tibetans has shown that they do not experience a deficiency in vitamin C, although their diet practically lacks fruits and vegetables. The vitamin activity of yak milk is quite high. Table 7 shows the composition and content of various vitamins in milk (3, 30-32).

Table 7. Content of antioxidant vitamins in yak and cow milk					
Types of milk	Vitamins, mg/100g				
	A, mcg/100	β- carotene,	Ε,	C, mg/100	PP,
	g	mcg/100 g	mcg/100 g	g	mg/100 g
Yak milk, Kyrgyzstan (31)	23.45 (6.2)	3.81 (0.76)	56.05 (9.6)	1.67 (0.25)	0.334 (0.037)
Yak milk, China (3)	13.88 (4.52)	-	30.15 (7.30)	3.28 (9.03)	0.00261 (0.0032)
Cattle milk (32)	37.0	16.0	80.0	1.0	0.13

The vitamin content of yak milk varies greatly among breeds and is different from cow's milk. Seasonal changes in yak food sources lead to changes in the vitamin content of yak milk (31). Studies have also shown that the content of vitamins A, E and C in yak milk depends on the altitude of the pasture where the animals live and increases with increasing altitude (32-34). Vitamin A cannot be synthesized by animals and must be obtained from food. This dependence of vitamin A content on the altitude of the animal, namely  $\beta$ -carotene, the main precursor of vitamin A, has been confirmed by other studies (35). Vitamin E reduces oxygen consumption and improves tissue oxygenation (36) and, thus, can increase the body's resistance to the hypoxic environment of highlands. The high content of vitamin E in the milk of yaks raised in the highlands and frequent consumption of milk are beneficial for the population of mountainous areas, since it is at high altitudes that oxygen deficiency is felt.

### Medicinal and functional properties of yak milk

Yak milk is rich in nutrients that can help maintain health. In addition, it includes special amino acid and fatty acid profiles, as well as high levels of antioxidant vitamins, specific enzymes and bacteria with probiotic activity, which provide it with numerous functional and medicinal properties (3, 35, 36).

In vitro and in vivo scientific studies conducted by scientists from different countries have shown that yak milk and its bioactive components have antioxidant, anticancer, antibacterial, antihypertensive, anti-inflammatory, hypocholesterolemic, antihypoxic, immunomodulatory, antidiabetic, tonic, laxative properties (37, 38). These properties provide prospects for the development of functional products with the addition of yak milk.

### Antioxidant properties

Oxidation of the body contributes to the production of Reactive oxygen species (ROS), which is the main cause of many chronic diseases (39, 40). Antioxidants are closely associated with anti-inflammatory, anticancer and immunomodulatory properties.

As a rule, the body's antioxidant system neutralizes ROS to maintain homeostasis.

When this purification system does not work sufficiently, oxidative stress occurs, leading to the emergence of pathological processes. Both natural compounds and synthetic drugs are used to activate the body's antioxidant system. In contrast, natural antioxidant peptides isolated from dairy products, including yak milk, have advantages in terms of safety, non-toxicity and increased bioavailability. Antioxidant peptides obtained from yak milk casein have the ability to interact with amino acids located in the catalytic centers of enzymes involved in oxidation processes in organisms. This makes it possible to reduce their activity and use such peptides for therapeutic purposes. In recent years, active research has been carried out aimed at obtaining peptides with pronounced antioxidant properties from yak milk casein in order to improve human health. Biologically active substances formed during the natural fermentation of milk with the participation of lactic acid bacteria demonstrate significant antioxidant potential.

In one study, trypsin and pepsin hydrolysis of milk casein filtrate (YCH) obtained in vitro was used, followed by an assessment of the ability to neutralize free radicals (DPPH and ABTS). The results showed that the formed peptides have high antioxidant activity. This confirms that peptides with a pronounced antioxidant effect can be isolated from yak milk casein, which opens up opportunities for obtaining natural antioxidants (41). Such peptides are able to reduce the level of oxidative stress and protect cells from damage (3).

In one study, the antioxidant properties of the T10 peptide obtained from yak milk, whey protein hydrolysate were studied in a model of human umbilical vein endothelial cell (HUVEC) injury caused by hydrogen peroxide. It was found that this peptide significantly reduces cellular damage, increases cell survival by regulating the expression of apoptotic genes bcl-2 and bax, as well as activating the antioxidant pathway Nrf2, which prevents apoptosis and enhances antioxidant defense (39, 42). Another study showed that the use of lactic acid bacteria in fermented yak milk significantly increased the activity of glutathione (GSH) and catalase (CAT) in the liver and serum of aging mice exposed to D-galactose. An increase in superoxide dismutase (SOD) activity in serum and brain was also observed, along with a decrease in malondialdehyde, indicating pronounced antioxidant activity (43). In addition, the Lactobacillus plantarum As21 strain, isolated from fermented yak milk, demonstrated antioxidant properties in the body of the nematode Caenorhabditis elegans and can be considered as a promising probiotic for slowing down the aging process (44).

## Anti-cancer properties

Oncological diseases are a serious obstacle to increasing human life expectancy. According to the World Health Organization in 2020, 19.3 million new cases of cancer and about 10 million cancer-related deaths were registered worldwide. Projections show that by 2040, the number of new cases could reach 27.5 million annually (45).

Today, there are many drugs for the treatment of cancer, but their high toxicity and side effects limit their use. This encourages researchers to search for effective and less toxic alternatives based on natural compounds (46).

Studies show that milk proteins are a promising source of biologically active peptides with antitumor potential (47). In particular, peptides isolated from yak milk casein exhibit a variety of biological effects. It was found that hydrolysates obtained using trypsin and alkaline protease have a pronounced ability to suppress the growth of breast cancer cells (MCF7 and MDA-MB-231). One of the isolated nanopeptides (TPVVVPPFL) showed a targeted inhibitory effect on tumor cells, inducing apoptosis and blocking their cell cycle (48). In addition, lactobacilli isolated from vak milk also showed a pronounced ability to suppress the growth of HeLa tumor cells, while not having a toxic effect on normal cells such as HEK293 (49). It was also found that polysaccharides produced by the Lactobacillus casei SB27 strain present in yak milk significantly inhibit the proliferation of colorectal cancer cells (HT-29 lines). This polysaccharide was found to enhance the expression of Bad, Bax, Caspase-3 and Caspase-8 genes in HT-29 cells (50, 51). These findings support the potential of yak milk as a source of functional food components with anticancer properties, including both peptides and probiotic strains, which can be used as natural anticancer agents.

It has also been shown that some proteins such as BgIFITM2 and BgIFITM3, expressed by genes found in yak milk, also possess anticancer activity (52). Although BgIFITM3 protein is mainly expressed in the liver, its presence in milk may also be associated with anticancer activity.

Yak milk and its derivatives contain bioactive components that are capable of inhibiting tumor growth, suggesting that they may be potential anticancer agents (3).

Studies have identified peptides such as TPVVVPPFL, VAPFPEVFGK, and MQELPYPY, derived from yak milk casein using trypsin and alkaline protease. These peptides exhibit anticarcinogenic properties and are mainly composed of hydrophobic amino acids such as Pro, Val, Phe, Leu, Ile, Ala and Gly, which increase their activity. Hydrophobicity is considered an important factor determining the effectiveness of such peptides in combating tumor cells (48).

In addition, the anticancer peptide TPVVVVVPPFL from yak milk casein inhibits the proliferation of MCF7 and MDA-MB-231 cells by inducing apoptosis through cell cycle arrest (48).

## **Antibacterial properties**

Yak milk contains three main components: yak milk peptides, lactic acid bacteria and their metabolites, which have high antibacterial activity (53). Two antibacterial peptides with the amino acid sequences Arg-Val-Met-Phe-Lys-Trp-Ala and Lys-Val-Ile-Ser-Met-Ile, obtained from yak milk protein hydrolysate, exhibit inhibitory activity against bacteria such as Bacillus subtilis, Staphylococcus aureus, Listeria innocua, Escherichia coli, Enterobacter cloacae and Salmonella paratyphi, and also suppress the growth of some fungi (54). Hydrolyzed yak milk casein also has pronounced antibacterial activity, effectively suppressing the growth of Escherichia coli, while not having a toxic effect on RAW 264.7 cells (55).

Yak milk also contains beneficial microorganisms that may enhance its antibacterial properties. The Y5-P1 strain isolated from fermented yak milk showed activity against both Gram-positive and Gramnegative bacteria, with minimum inhibitorv concentrations ranging from 62.5 to 250  $\mu$ g/mL (56). In vivo studies also support the antibacterial potential of yak milk lactic acid bacteria. For example, Lactobacillus reuteri isolated from vak milk demonstrated good activity against Escherichia coli. Supplementation with these bacteria improved the gut microbiota and reduced infection-induced weight loss (57, 58), suggesting that vak milk-derived probiotics may improve gut health. In addition, bacteriocins produced by Lactobacillus plantarum SHY 21-2 and exopolysaccharides isolated from Streptococcus thermophilus ZJUIDS-2-01 demonstrated good antibacterial properties (59, 60).

## Antihypertensive properties

Hypertension is a major public health problem, representing a major risk factor for CV diseases such as stroke, myocardial infarction and heart failure.

Bioactive peptides extracted from dietary proteins are widely used to treat hypertension, with their mechanisms of action involving inhibition of angiotensin-converting enzyme (ACE) (61-65) ACE is a key element of the renin-angiotensin-aldosterone system, which regulates blood pressure and CV health (64). Clinical studies show that ACE inhibitors such as captopril, lisinopril and enalapril can reduce CV mortality by 12%.

Yak milk is one of the sources of such antihypertensive peptides, for example, KYIPIQ peptide purified from yak milk casein exhibits potent ACE inhibitory activity and holds promise for the development of therapeutic agents for the treatment of hypertension (65). In vitro studies have shown that KYIPIQ peptide enhances nitric oxide (NO) synthesis and endothelial nitric oxide synthase (eNOS) expression in human vascular endothelial cells. In addition, the amino acid sequences of peptides such as YQKFPQY, LPQNIPPL, SKVLPVPQK, LPYPYY, and FLPYPYY obtained from yak milk casein hydrolysates are consistent with the known bioactive peptides in cow's milk protein, confirming the antihypertensive potential of yak milk (65, 66). Peptides PPEIN, PLPLL, SLVYPFPGPI, KFPQY, MPFPKYP, MFPPQ, QWQVL, PFPGPIPN and LPLPLL obtained from hydrolyzed yak milk proteins have ACE inhibitory activity and can be used to develop new antihypertensive drugs (14, 67).

In addition, the fatty acid profile of yak milk is considered to be beneficial for nutrition, as it is low in SFA and high in MUFA and PUFA, which help reduce the risk of CV diseases and improve lipid metabolism (67-69).

## Anti-inflammatory properties

Inflammation serves as the primary mechanism by which the body defends itself against microbial invasion. This process can ultimately lead to conditions such as diabetes, neurodegenerative disorders, Parkinson's disease, CV disease, and various types of cancer in humans (2). Scientists have found that the anti-inflammatory peptide casein from yak milk treats inflammation by inhibiting the antiinflammatory factors interleukin-6 (IL-6), interleukin-1 $\beta$  (IL-1 $\beta$ ), and tumor necrosis factor alpha (TNF- $\alpha$ ) (70).

## **Tonic properties**

Recent studies have shown that yak collagen peptides have a significant anti-fatigue effect in mice (71). Oral administration of yak milk powder can dosedependently increase the forced swimming time in mice, as well as increase liver glycogen levels, decrease serum triglyceride concentrations, and decrease lactate and urea levels, which are usually elevated after exercise (72). This indicates the ability of yak milk to enhance endurance and reduce fatigue. *Lactobacillus fermentum* HFY03, isolated from fermented yak milk, has shown good anti-fatigue and antioxidant properties in in vivo experiments. Administration of this strain to ICR mice for 4 weeks increased the swimming time to exhaustion, decreased urea nitrogen and lactate levels, and also contributed to an increase in the content of fatty acids and glycogen in the liver, and a decrease in the activities of alanine aminotransferase, creatine kinase, and aspartate aminotransferase in serum.

In addition, HFY03 decreased the levels of MDA, CAT, and SOD (73). The anti-fatigue properties of Lactobacillus fermentum HFY03 are associated with improved liver glycogen storage, decreased lactate accumulation, decreased protein breakdown, and increased fat utilization. Although there are not many studies in this area, the effectiveness of yak milk and its derivatives in combating fatigue is significant. In the future, this milk may become the basis for the creation of products that will be useful for groups such as the elderly and athletes.

## Laxative properties

Constipation is a common gastrointestinal disorder, and the effect of probiotics on its treatment has been actively studied in both animals and humans (74). Some studies suggest that probiotics contained in yak milk can improve constipation. Lactobacillus fermentum Lee (LF-Lee), isolated from yak milk, has a positive effect on activated carbon-induced constipation in ICR mice. After nine days of oral administration of LF-Lee, mice showed a significant increase in serum levels of MTL, Gas, ET, AChE, SP, and VIP, while SS levels were significantly reduced (75). Similarly, Lactobacillus fermentum YS2 and Lactobacillus plantarum YS-3 isolated from yak yogurt also improved activated carbon-induced constipation in Kunming mice (76, 77).

## Hypocholesterolemic properties

Studies have shown that probiotics can significantly reduce cholesterol levels. Some probiotics derived from yak milk and yogurt have been confirmed to have a similar effect. For example, Lactobacillus casei YBJ02 exhibits an inhibitory effect on the increase in blood lipid levels in mice with hyperlipidemic mice. YBJ02 helps to reduce cholesterol levels in the liver and feces of hyperlipidemic mice, reduces triglycerides (TG), total cholesterol (TC) and LDL in serum, and increases HDL. The mechanism of this effect is to inhibit lipid accumulation through regulation of the synthesis of intestinal flora genes and obesity processes (78).

It was also found that Lactobacillus plantarum Lp3, isolated from yak milk, demonstrates more pronounced cholesterol-lowering properties in vitro experiments. In hyperlipidemic rats, Lp3-fed rats significantly reduced

both serum and liver cholesterol and triglyceride levels, and decreased liver lipid deposition (42).

These results suggest that YBJ02 and Lp3 may be promising probiotics for the treatment of hyperlipidemia, and yak milk may be a valuable source for the development of cholesterol-lowering drugs.

### Antihypoxic properties

Yak milk is an important food product for high-altitude residents, and studies have confirmed its ability to resist hypoxia. In a hypoxic mouse model, yak milk powder was found to prolong the survival time of animals under hypoxic conditions, as well as improve their red blood cell and hemoglobin levels. Compared with regular cow's milk, yak milk has a more pronounced antihypoxic activity (79). In vitro experiments showed that bta-miR-34a, which is expressed in yak milk extracellular vesicles, has a protective effect on the survival of IEC-6 cells under hypoxia and can reduce hypoxic intestinal injury (80). These results indicate that yak milk may be a novel functional food ingredient with antihypoxic properties.

## Immunostimulatory properties

In recent years, increased attention has been focused on the immune system due to the increase in chronic and other health-related diseases. Immunomodulatory drugs currently in development are expensive and have adverse effects on human physiology. International researchers have studied the immunomodulatory properties of peptides derived from yak milk casein through various approaches, including cell culture and in vitro methods. Yak milk not only provides abundant energy and nutrients, but also contains many immunoactive substances such as immunoglobulin, insulin growth factor, and epidermal growth factor. The contents of immunoglobulin A (IgA), IgG, and IgM are higher than those of other mammalian milk, and the levels of IgA and IgG are approximately 1.5 times higher than those of human milk (81, 82).

Immunomodulatory peptides from yak milk casein modulate physiological functions by assisting T cell differentiation, regulating Th1/Th2 balance, and modulating intestinal FeSO 4 solubility, indicating potential therapeutic applications in cellular immunity disorders (72). Mao et al. (70) reported that hydrolysates obtained by hydrolysis of yak milk casein with Alcalase exhibited enhanced immunomodulatory activity, increased hydrolysis extent, and increased peptide yield.

Further studies may reveal additional multifunctional activities in yak milk casein, such as potential roles in osteoporosis prevention and cholesterol lowering, which are currently not well documented (39).

## Antidiabetic properties

The incidence of type 2 diabetes mellitus (T2DM) is increasing worldwide, and China currently leads the world in diabetes cases, affecting more than 94 million people (83). Recently, peptides derived from natural food proteins known for their antidiabetic properties have attracted considerable attention of researchers. According to Li et al. (82), the antidiabetic peptide RK7 (IC 50 = 0.45 mg/mL) was isolated from yak cheese. Antidiabetic peptides mainly act through two mechanisms: inhibiting DPP-IV, which regulates insulin secretion, and suppressing  $\alpha$ -glucosidase or  $\alpha$ -amylase to regulate or delay glucose absorption in the small intestine, thereby reducing postprandial hyperglycemia (84). Antidiabetic peptides derived from milk can treat diabetes by inhibiting dipeptidyl peptidase-IV (DPP- $\alpha$ -glucosidase and  $\alpha$ -amylase, but IV), only antidiabetic peptides RPKHPIK (RK7) and KVLPVPQ (KQ7), which can inhibit  $\alpha$ -amylase, have been identified in yak milk casein (41).

## Current knowledge and future research directions

To date, there is sufficient scientific data confirming the high nutritional and biological value of yak milk. It is rich in proteins, fats, vitamins (A, D, group B), minerals (calcium, iron, zinc), as well as biologically active substances - oligosaccharides, peptides, polyphenols and conjugated linoleic acid (CLA). These components give milk potential antioxidant, antiinflammatory, immunomodulatory and antibacterial properties.

There is evidence that regular consumption of yak milk can improve the state of intestinal microflora, strengthen the immune system and reduce the risk of chronic diseases. The possibility of using yak milk to create functional products and nutraceuticals is also being considered.

However, many questions remain open. The main areas of future research include:

• Clarification of the composition of milk depending on the breed, conditions of maintenance, season and processing technology.

• Study of the action of individual components at the cellular and molecular level.

• Clinical studies involving various population groups (children, the elderly, patients with chronic diseases).

• Development of new products (e.g. yoghurts, fermented drinks, dry mixes) and assessment of their benefits.

• Study of safety during long-term use and possible interactions with drugs.

• Analysis of the potential for using yak milk in medicine, sports and therapeutic nutrition.

For further development of this area, an integrated approach is needed involving specialists in various fields - from nutritionists to technologists. This will help to better understand the properties of yak milk and use it in modern nutrition and healthcare systems.

## Conclusions

Yak milk is a valuable product with a high content of nutrients with medicinal and functional properties. This milk is significantly more beneficial for health compared to traditional cow's milk due to its balanced composition.

Yak milk is an excellent source of amino acids, minerals and unsaturated fatty acids. Its amino acid composition is better balanced than that of cow's milk, and the level of omega-3 and omega-6 fatty acids is significantly higher. This helps to normalize metabolism, maintain CV health and improve the overall health of the body.

It is rich in calcium, magnesium, phosphorus and potassium, which helps strengthen bones, improve the nervous system and maintain normal muscle function. These trace elements play a key role in maintaining overall health and physical activity.

Yak milk has a wide range of functional and medicinal properties, which makes it valuable not only as a food product, but also as a natural preventive measure. In vitro and in vivo studies have confirmed its antioxidant, anti-cancer, antibacterial, antiinflammatory, antihypertensive, hypocholesterolemic, antihypoxic, immunomodulatory and antidiabetic properties. These properties make yak milk useful for the prevention and treatment of various diseases.

Yak milk is especially valuable as a source of biologically active substances, including peptides, probiotic microorganisms and beneficial fatty acids. These components help improve intestinal microflora, strengthen the immune system and increase the absorption of nutrients. It is also worth noting that yak milk neutralizes free radicals and reduces inflammatory processes in the body, which can be useful for the prevention of chronic diseases.

Despite the research conducted, many issues related to the milk of Kyrgyz yaks remain poorly understood. Additional research is needed to fully reveal the benefits of yak milk and its potential in the medical and food industries. This will clarify the mechanisms of action of milk and conduct clinical trials aimed at assessing its effectiveness for human health.

For the effective use of yak milk in mass production, it is necessary to develop new technologies for processing and storing this product. It is important to solve the problems associated with the inaccessibility of raw milk, as well as to increase the interest of yak breeders, especially in Kyrgyzstan, in the extraction and sale of yak milk. The creation of infrastructure for its production and processing, as well as training farmers and workers of processing enterprises, facilitating more efficient use of this unique raw material, will be a key step in the development of the market. Popularization of yak milk and its processed products in the domestic and international markets will play an important role in increasing consumer demand. This, in turn, will contribute to the expansion of the range of healthy and functional food products, as well as support the economy of Kyrgyzstan. Ultimately, yak milk can become an important element of the global context of healthy nutrition, offering consumers not only healthy but also environmentally friendly products.

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## References

1.Haimei Li, Ying Ma, Qiming Li, Jiaqi Wang, Jinju Cheng, Jun Xue et al. The chemical composition and nitrogen distribution of Chinese yak (maiwa) milk. Int J Mol Sci 2011; 4885-95.

2.Cao JY, Dong Q, Wang ZY, Mei LJ, Tao YD, Yu RT. Three pairs of novel enantiomeric 8-o-4' type neolignans from saussurea medusa and their antiinflammatory effects in vitro. Int J Mol Sci 2022; 23: 14062. doi: 10.3390/ijms232214062

3.Wang D, Zhou Y, Zheng X, Guo J, Duan H, Zhou S, Yan W. Yak milk: nutritional value, functional activity, and current applications. Foods 2023; 12: 2090. doi: 10.3390/foods12112090

4.Ma Y, He S, Park YW. Yak Milk. In: Handbook of Milk of Non-Bovine Mammals. John Wiley & Sons: Hoboken, NJ, USA, 2017; Pp. 481–513.

5.Cao M, Huang L, Jin S, Zhao M, Zheng Y. Comparative proteomics study of yak milk from standard and naturally extended lactation using iTRAQ technique. Animals (Basel) 2022; 12: 391. doi: 10.3390/ani12030391

6.Saalieva AN, Usubalieva AM, Musulmanova MM. Feeding ration of yaks of the Kyrgyz population and its influence on the biochemical composition of milk. Food Systems 2024; 7: 91–8. Doi: 10.21323/2618-9771-2024-7-1-91-98

7.Bakhtushkina AI, Koval AD. Milk yield and chemical composition of milk of yakih of the Altai population. Bull Altai Agrarian University 2020: 8;. 81-6.

8.Elemanova RSh. Characteristics of seasonal changes in the protein composition of haynak milk. Equip Technol Food Product 2022; 52: 555–69.

9.Barsila SR. Effect of parity in different grazing seasons on milk yield and composition of cattle × yak hybrids in the Himalayan alpines. J Applied Animal Res 2019; 47: 591–6. Doi: 10.1080/09712119.2019.1697274

10. Al Haj OA, Al Kanha HA. Compositional, technological and nutritional aspects of dromedary camel milk. Int Dairy J 2010; 20: 811-21. doi.org/10.1016/j.idairyj.2010.04.003

11.Li H. Protein composition of yak milk. Dairy Sci Technol 2010; 90: 111–7. Doi: 10.1051/dst/2009048

12.Bai WL, Yin RH, Dou QL, Jiang WQ, Zhao SJ, Ma ZJ, et al. Molecular characterization and phylogenetic analysis of a yak (Bos grunniens) κ-casein cDNA from lactating mammary gland. Mol Biol Re 2011; 38: 2711-8. doi: 10.1007/s11033-010-0414-6

13.Qu X, Cui Y, Yu T, Hu T, Wang C, Lv X et al. Detection of  $\alpha$ S2-casein variants in Chinese yak (Bos grunniens) by PCR-SSC. J Genet 2015; 94: e1-4. doi: 10.1007/s12041-015-0468-2

14. Lin K, Zhang L, Han X, Meng Z, Zhang J, Wu Y, et al. Quantitative structure-activity relationship modeling coupled with molecular docking analysis in screening of angiotensin i-converting enzyme inhibitory peptides from qula casein hydrolysates obtained by two-enzyme combination hydrolysis. J Agric Food Chem 2018; 66: 3221-8. doi: 10.1021/acs.jafc.8b00313

15.Lin K, Zhang LW, Han X, Xin L, Meng ZX, Gong PM et al. Yak milk casein as potential precursor of angiotensin I-converting enzyme inhibitory peptides based on in silico proteolysis. Food Chem 2018; 254: 340-7. doi: 10.1016/j.foodchem.2018.02.051

16. Roin NR, Larsen LB, Comi I, Devold TG, Eliassen TI, Inglingstad RA, et al. Identification of rare genetic variants of the  $\alpha$ S-caseins in milk from native Norwegian dairy breeds and comparison of protein composition with milk from high-yielding Norwegian Red cows. J Dairy Sci 2022; 105: 1014-27. doi: 10.3168/jds.2021-20455 17.Bär C, Sutter M, Kopp C, Neuhaus P, Portmann R, Egger L, et al. Impact of herbage proportion, animal breed, lactation stage and season on the fatty acid and protein composition of milk. Int Dairy J 2020; 109: 104785. Doi: 10.1016/j.idairyj.2020.104785

18.Li S, Ye A, Singh H. Seasonal variations in composition, properties, and heat-induced changes in bovine milk in a seasonal calving system. J Dairy Sci 2019; 102: 7747-59. doi: 10.3168/jds.2019-16685

19. Vanbergue E, Delab JL, Peyraud S, Gallard GY, Hurtaud C. Effects of breed, feeding system, and lactation stage on milk fat characteristics and spontaneous lipolysis in dairy cows. J Dairy Sci 2017; 100: 4623-36. doi: 10.3168/jds.2016-12094

20.FAO/WHO/UNU (2002:Geneva, Switzerland) Protein and amino acid requirements in human nutrition : report of a joint FAO/WHO/UNU expert consultation. Available at: URL: www.who.int

21.Silanikove N, Leitner G., Merin U. Non-bovine milk and milk products. Doi: 10.1016/B978-0-12-803361-6.00004-1

22.Saalieva AN. Analysis of fatty acid composition of yachiha milk. Bulletin of KRSU 2022; 3: 180.

23.Saalieva A. Analysis of fatty acid composition of yak milk. Bulletin of KRSU 2022; 3: 154-61. DOI: 10.36718/1819-4036-2022-3-154-161

24.Guzeev Yu.V. Composition of fatty acids in milk of different types of farm animals. Bull Sumy Nat Agrarian University 2016; 5: 148-56.

25.Liu HN, Ren FZ, Jiang L, Ma ZL, Qiao HJ, Zeng SS, Gan BZ, Guo HY. Fatty acid profile of yak milk from the Qinghai-Tibetan Plateau in different seasons and for different parities. J Dairy Sci 2011; 94: 1724-31. doi: 10.3168/jds.2010-3749

26.He S, He Y, Ma J, Wang Q, Li X, Yang S, et al. Milk fat chemical composition of yak breeds in China. j Food Compos Analysis 2011; 24: 223-30. DOI:10.1016/j.jfca.2010.07.008

27.Abdullah MM, Jew S, Jones PJ. Health benefits and evaluation of healthcare cost savings if oils rich in monounsaturated fatty acids were substituted for conventional dietary oils in the United States. Nutr Rev 2017; 75: 163-74. doi: 10.1093/nutrit/nuw062

28.Cherevko AI. Encyclopedia of nutrition in 9 volumes. Volume 3. M.: KnoRus. 2019. pp. 736

29.Chen L. Analysis of 17 elements in cow, goat, buffalo, yak, and camel milk by inductively coupled plasma Mass Spectrometry (ICP-MS). Royal Soc Chem 2020; 6736–42.

30.Usubalieva A, Muslimova M. Seasonal changes in the micronutrient composition of milk of yak breeders of the Kyrgyz population. Sci Res Kyrgyz Republic 2024; 3: 49-60.

31.Verduci E, D'Elios S, Cerrato L, Comberiati P, Calvani M, Palazzo S et al. Cow's milk substitutes for children: nutritional aspects of milk from different mammalian species, special formula and plant-based beverages. Nutrients 2019; 27; 11: 1739. doi: 10.3390/nu11081739

32.Luo J, Wang ZW, Song JH, Pang, R, Ren FZ. Lipid composition of different breeds of milk fat globules by confocal raman microscopy. Guang Pu Xue Yu Guang Pu Fen Xi 2016; 36: 125–9.

33.Yang L, Yang C, Chi F, Gu X, Zhu Y. A survey of the vitamin and mineral content in milk from yaks raised at different altitudes. Int J Food Sci 2021; 2021: 1855149. doi: 10.1155/2021/1855149

34.Cui GX, Yuan F, Degen AA, Liu SM, Zhou JW, Shang ZH, et al. Composition of the milk of yaks raised at different altitudes on the Qinghai–Tibetan plateau. Int Dairy J 2016; 59: 29–35.

35. Guo XS, Ding LM, Long RJ, Qi B, Shang ZH, Wang Y, et al. Changes of chemical composition to high altitude results in Kobresia littledalei growing in alpine meadows with high feeding values for herbivores. Anim Feed Sci Technol 2012; 173, 186-93. Doi: 10.1016/j.anifeedsci.2012.01.011

36.Jafari T, Fallah AA, Reyhanian A, Sarmast E. Effects of pomegranate peel extract and vitamin E on the inflammatory status and endothelial function in hemodialysis patients: a randomized controlled clinical trial. Food Funct 2020; 11: 7987-93. doi: 10.1039/d0fo01012j

37. Guo X, Long R, Kreuzer M, Ding L, Shang Z, Zhang Y, et al. Importance of functional ingredients in yak milk-derived food on health of Tibetan nomads living under high-altitude stress: a review. Crit Rev Food Sci Nutr 2014; 54: 292-302. doi: 10.1080/10408398.2011.584134

38.Kalwar Q, Ma X, Xi B, Korejo RA, Bhuptani DK, Chu M, et al. Yak milk and its health benefits: a comprehensive review. Front Vet Sci 2023; 10: 1213039. doi: 10.3389/fvets.2023.1213039

39.Wang W, Liang Q, Zhao B, Chen X, Song X. Functional peptides from yak milk casein: biological activities and structural characteristics. Int J Mol Sci 2024; 25): 9072. doi: 10.3390/ijms25169072 40.Ji M, Gong X, Li X, Wang C, Li M. Advanced research on the antioxidant activity and mechanism of polyphenols from hippophae species-a review. Molecules 2020; 25: 917. doi: 10.3390/molecules25040917

41.Liu Q, Yang M, Zhao B, Yang F. Isolation of antioxidant peptides from yak casein hydrolysate. RSC Adv 2020; 10: 19844-51. doi: 10.1039/d0ra02644a

42.Yang BJ, Liang, Q. Advances on the structureactivity relationship of bioactive peptides in cheese. Food Ferment Ind 2021: 47; 288–93.

43.Ding W. Screening for lactic acid bacteria in traditional fermented Tibetan yak milk and evaluating their probiotic and cholesterol-lowering potentials in rats fed a high-cholesterol diet. J Function Foods 2017; 32: 324-32.

44.Li W, Zhao Z, Chen D, Peng Y, Lu Z. Prevalence and associated factors of depression and anxiety symptoms among college students: a systematic review and meta-analysis. J Child Psychol Psychiat 2022; 3: 1222-30. doi: 10.1111/jcp13606

45.Deng H, Liu J, Xiao Y, Wu JL, Jiao R. Possible mechanisms of dark tea in cancer prevention and management: A comprehensive review. Nutrients 2023; 15: 3903. Doi: 10.3390/nu15183903

46.Khalifa SAM, Elias N, Farag MA, Chen L, Saeed A, Hegazy MF, et al. Marine natural products: a source of novel anticancer drugs. Mar Drugs 2019; 17: 491. doi: 10.3390/md17090491

47.Sah BNP, Vasiljevic T, McKechnie S, Donkor ON. Identification of anticancer peptides from bovine milk proteins and their potential roles in management of cancer: A critical review. Compr Rev Food Sci Food Saf 2015; 14:123-38. doi: 10.1111/1541-4337.12126

48.Gu H, Liang L, Zhu Z, Mao X. Preparation and identification of anti-breast cancer cells peptides released from yak milk casein. Front Nutr 2022; 9: 997514. doi: 10.3389/fnut.2022.997514

49.Kaur M, Singh H, Jangra M, Kaur L, Jaswal P, Dureja C, Nandanwar H, et al. Lactic acid bacteria isolated from yak milk show probiotic potential. Appl Microbiol Biotechnol 2017; 101: 7635-52. doi: 10.1007/s00253-017-8473-4

50.Wang H, Wang L, Li J, Fu F, Zheng Y, Zhang L. Molecular characterization, expression and functional analysis of yak IFITM3 gene. Int J Biol Macromol 2021; 184: 349-57. doi: 10.1016/j.ijbiomac.2021.06.057

51.Di W, Zhang L, Wang S, Yi H, Han X, Fan R, et al. Physicochemical characterization and antitumor activity of exopolysaccharides produced by Lactobacillus casei SB27 from yak milk. Carbohydr Polym 2017; 171: 307-15. doi: 10.1016/j.carbpol.2017.03.018 52.Wang H, Wang L, Luo X, Guan J, Zhang X, Zhang L, et al. Molecular characterization, expression and antitumor function analysis of yak IFITM2 gene. Int J Biol Macromol 2022; 209: 405-12. doi: 10.1016/j.ijbiomac.2022.03.212

53.Xuan J, Feng W, Wang J, Wang R, Zhang B, Bo L, et al. Antimicrobial peptides for combating drugresistant bacterial infections. Drug Resist Update 2023; 68: 100954. doi: 10.1016/j.dru2023.100954

54.Pei J, Jiang H, Li X, Jin W, Tao Y. Antimicrobial peptides sourced from post-butter processing waste yak milk protein hydrolysates. AMB Express 2017; 7: 217. doi: 10.1186/s13568-017-0497-8

55. Cheng, X. Tang XQ, Wang, Mao XY. Antibacterial effect and hydrophobicity of yak κ-casein hydrolysate and its fractions International Dairy Journal. 2013; 31: 111-6.doi: 10.1016/j.idairyj.2012.12.004

56.Kaur M, Jangra M, Singh H, Tambat R, Singh N, Jachak SM, et. al. Pseudomonas koreensis recovered from raw yak milk synthesizes a  $\beta$ -carboline derivative with antimicrobial properties. Front Microbiol 2019; 10: 1728. doi: 10.3389/fmicb.2019.01728.

57.Wang Y, Li A, Zhang L, Waqas M, Mehmood K, Iqbal M, et al. Probiotic potential of Lactobacillus on the intestinal microflora against Escherichia coli induced mice model through high-throughput sequencing. Microb Pathog 2019; 137: 103760. doi: 10.1016/j.micpath.2019.103760

58.Ali SM, Salem FE, Aboulwafa MM, Shawky RM. Hypolipidemic activity of lactic acid bacteria: Adjunct therapy for potential probiotics. PLoS One 2022; 17: e0269953. doi: 10.1371/journal.pone.0269953

59.Cao F, Liang M, Liu J, Liu Y, Renye JA Jr, Qi PX, Ren D. Characterization of an exopolysaccharide (EPS-3A) produced by Streptococcus thermophilus ZJUIDS-2-01 isolated from traditional yak yogurt. Int J Biol Macromol 2021; 192: 1331-43. doi: 10.1016/j.ijbiomac.2021.10.055

60.Peng S, Song J, Zeng W, Wang H, Zhang Y, Xin J, et al. A broad-spectrum novel bacteriocin produced by Lactobacillus plantarum SHY 21–2 from yak yogurt: Purification, antimicrobial characteristics and antibacterial mechanism. LWT 2021; 142: 110955. DOI: 10.1016/j.lwt.2021.110955

61.Sánchez D, Kassan M, Contreras Mdel M, Carrón R, Recio I, Montero MJ, et al. Long-term intake of a milk casein hydrolysate attenuates the development of hypertension and involves cardiovascular benefits. Pharmacol Res 2011; 63: 398-404. doi: 10.1016/j.phrs.2011.01.015

62.Singh T, Arora S., Sarkar M. Yak milk and milk products: Functional, bioactive constituents and therapeutic potential. Int Dairy J 2023; 142: 105637.

63.Xue L, Yin R, Howell K, Zhang Activity and bioavailability of food protein-derived angiotensin-l-converting enzyme-inhibitory peptides. Compr Rev Food Sci Food Saf 2021; 20: 1150-87. doi: 10.1111/1541-4337.12711

64.Bader M. Tissue renin-angiotensin-aldosterone systems: Targets for pharmacological therapy. Ann Rev Pharmacol and Toxicol 2010; 50: 439-65.

65.Lin K. ACE inhibitory peptide KYIPIQ derived from yak milk casein induces nitric oxide production in HUVECs and diffuses via a transcellular mechanism in Caco-2 monolayers. Proc Biochemistr 2020; 99: 103-11.

66.Abedin MM, Chourasia R, Chiring Phukon L, Singh SP, Kumar Rai A. Characterization of ACE inhibitory and antioxidant peptides in yak and cow milk hard chhurpi cheese of the Sikkim Himalayan region. Food Chem 2022; 13: 100231. doi: 10.1016/j.fochx.2022.100231

67.Wang, Z, Liu, W, Gao, Y, and Xu, X. Comparative study of the physicochemical properties and fatty acid profiles of yak and cow milk from the Tibetan Plateau. J Food Compost Anal 202; 100: 103977. doi: 10.1016/j.jfca.2021.103977425

68.Wang, Y, Chen, X, Guo, J, Liu, X, and Ren, F. Nutrient composition of yak milk from the Qinghai-Tibet Plateau in China. Food Science Nutr 2021; 9: 2224–34. doi: 10.1002/fsn3.2208432

69.Xu, Q, Fu, Y, Liu, Y, Xu, Y, Ding, L. Characterization of yak milk fat globules: comparison to small ruminants and mare milk. J Dairy Sci 2015; 98: 5385–400. doi: 10.3168/jds.2015-9357

70. Mao XY, Cheng X, Wang X, Wu SJ. Free-radicalscavenging and anti-inflammatory effect of yak milk casein before and after enzymatic hydrolysis. Food Chemistry 2011; 126: 484-90. Doi: 10.1016/j.foodchem.2010.11.025

71.Feng R, Zou X, Wang K, Liu H, Hong H, Luo Y. Antifatigue and microbiome reshaping effects of yak bone collagen peptides on Balb/c mice. Food Bioscience 2023; 52: 102447. doi: 10.1007/s13594-014-0198-x

72.Zhang W, Cao J, Wu S. Anti-fatigue effect of yak milk powder in mouse model. Dairy Sci Technol 2015; 95: 245-5. Doi: 10.1007/s13594-014-0198-x

73.Zhang J, Chen L, Zhang L, Chen Q, Tan F, Zhao X. Effect of Lactobacillus fermentum HFY03 on the antifatigue and antioxidation ability of running exhausted mice. Oxid Med Cell Longev 2021; 2021: 8013681. doi: 10.1155/2021/8013681

74.Dimidi E, Christodoulides S, Scott SM, Whelan K. Mechanisms of action of probiotics and the gastrointestinal microbiota on gut motility and constipation. Adv Nutr 2017; 8: 484-94. doi: 10.3945/an.116.014407

75.Qian Y, Suo H, DU M, Zhao X, Li J, Li GJ, et al. Preventive effect of Lactobacillus fermentum Lee on activated carbon-induced constipation in mice. Exp Ther Med 2015; 9: 272-8. doi: 10.3892/etm.2014.2064

76.Zhao X, Yi R, Qian Y, Park KY. Lactobacillus plantarum YS-3 prevents activated carbon-induced constipation in mice. J Med Food 2018; 21: 575-84. doi: 10.1089/jmf.2017.4109

77.Zhao X, Qian Y, Li G, Yi R, Park KY, Song JL. Lactobacillus plantarum YS2 (yak yogurt Lactobacillus) exhibited an activity to attenuate activated carboninduced constipation in male Kunming mice. J Dairy Sci 2019; 102: 26-36. doi: 10.3168/jds.2018-15206

78.Qian Y, Li M, Wang W, Wang H, Zhang Y, Hu Q, et al Effects of lactobacillus casei ybj02 on lipid metabolism in hyperlipidemic mice. J Food Sci 2019; 84: 3793-803. doi: 10.1111/1750-3841.14787

79.Zhang W. A preliminary study on anti-hypoxia activity of yak milk powder in vivo. Dairy Sci Technol 2014; 94: 633-9.

80.Gao HN, Ren FZ, Wen PC, Xie LX, Wang R, Yang ZN, et al. Yak milk-derived exosomal microRNAs regulate intestinal epithelial cells on proliferation in hypoxic environment. J Dairy Sci 2021; 104: 1291-303. doi: 10.3168/jds.2020-19063

81.Hock A, Miyake H, Li B, Lee C, Ermini L, Koike Y, et al. Breast milk-derived exosomes promote intestinal epithelial cell growth. J Pediatr Surg 2017; 52: 755-9. doi: 10.1016/j.jpedsurg.2017.01.032

82.Li A, Liu C, Han X, Zheng J, Zhang G, Qi X, et al. Tibetan Plateau yak milk: A comprehensive review of nutritional values, health benefits, and processing technology. Food Chem X 2023; 20: 100919. doi: 10.1016/j.fochx.2023.100919

83. Ćorković I, Gašo-Sokač D, Pichler A, Šimunović J, Kopjar M. Dietary polyphenols as natural inhibitors of  $\alpha$ -amylase and  $\alpha$ -glucosidase. Life (Basel) 2022; 12: 1692. doi: 10.3390/life12111692

84.Oseguera-Toledo ME, de Mejia EG, Amaya-Llano SL Hard-to-cook bean (Phaseolus vulgaris L.) proteins hydrolyzed by alcalase and bromelain produced bioactive peptide fractions that inhibit targets of type-2 diabetes and oxidative stress. Food Research Int 2015.; 76: 839-51.