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Mare's milk as a prospective functional product

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BACKGROUND

Food has a significant effect on health. The relationship between diet and health develops the importance of expanding functional food product research. Kazakhstan has a huge potential for functional products, such as saumal or mare's milk [1]. Throughout the ages, saumal has been used as an antidote because of its ability to excrete toxins. Today, saumal is used for pulmonary tuberculosis, anemia, rickets, diabetes mellitus, obesity, nerve diseases, inflammatory diseases of the stomach, and intestines. Saumal is called a longevity drink.

Mare's milk ("saumal") is a physiological, delicate, and easily assimilated biologically active product [1]. The composition of the mare's milk is similar to that of human milk and has a set of beneficial properties on our body, improving the functioning of the systems. Usually, mare's milk is used both fresh and fermented. Fermented milk is called in some countries koumiss, in Mongolia–ayrak [6].

Mare's milk contains about 40 biological components necessary for the human body: amino acids, fats, enzymes (lysozyme, amylase), microelements (calcium, sodium, potassium, phosphorus, iron, magnesium, copper, iodine, sulfur, cobalt, zinc, bromine) and vitamins (A, C, B1, B2, B6, B12, E, H, PP, beta-carotene, folic acid...) in optimally balanced proportions [1].

The mare's milk is characterized by a large amount of lactose (72.80 g / l, 0.03 s) and a reduced fat content (6.40 g / l; 04 sd) and proteins (caseins) (15.52 g / l, 0.11 s), especially caseins (13.4 g / l, 0.04 s) [1]. The milk in its composition belongs to the albumin group. While the milk of other domestic animals (with the exception of the donkeys) refers to the casein group. Albumin and casein are types of protein, giving the milk a distinctive white color [1]. Their difference lies in the fact that casein has a coarser (coarsely dispersed) structure and due to this fact is poorly

absorbed. Albumin, like the underlying globulin of mother's milk, is a finely dispersed (whey) protein and is digested easier. Mare's milk also contains about 50% of casein and about 39% of whey protein, while cow's milk contains about 80% of casein [2].

Milk is a unique source of vitamins A, B1, B6, B12, C, D, E, K and minerals (Fe, Cu, Mg, Mn, Zn and Ca) [2]. According to the mineral composition of the mare, milk is very close to the maternal [3]. The mare's milk contains important amino acids for our body, such as tryptophan, tyrosine and casein [4]. As for fat, the fat contained in mare's milk is almost the best animal fat in nature. Due to the specific finely dispersed structure, it is emulsified as quickly as possible (cleaved) and absorbed. A large percentage of all fats are composed of polyunsaturated fatty acids omega 3 and 6 [2, 3, 5].

There are a number of proteins found in mare's milk. When digested, these proteins release bioactive peptides with many different properties. These include blood pressure regulators, antimicrobial, and anti-inflammatory peptides [6, 7]. Lactation of mares begins with colostrum within the first seven days after the birth. The composition of milk varies in the number and content of certain nutrients and lasts until foals are weaned at the age of 5 to 8 months. The limiting factor in the production of mare's milk is a small volume of the breast (<2 L), which requires several daily milking (5-7 times / day) distributed in intervals of 2 to 3 hours [8].

The therapeutic significance of mare's milk was has been known throughout the territory of Russia and Western Asia [9]. Mongolian medicine used mare's milk for the treatment of chronic hepatitis and peptic ulcer disease [9]. Milk also has anti-acid properties due to the high content of phospholipids and vitamin A. The use of mare's milk for the treatment of patients with tuberculosis has been practiced for a long time in the territory of Russia and Mongolia. The therapeutic effect is associated with an increase in the number of erythrocytes and lymphocytes to the normal level (sedimentation rate) of erythrocytes [9].

Chen Y. and his colleagues report that koumiss is rich in protein ACE inhibitors (angiotensin-converting enzyme) that is involved in the regulation of the blood pressure. From koumiss, 4 proteins were isolated and purified: P_I, P_K, P_M, and P_P. The P_I protein is a part of the β-casein in mare's milk, the P_K protein corresponds to f144-150 of the cytochrome C-type protein NrfB, and the P_M and P_P proteins do not correspond to more than one milk protein from the NCBI database. All 4 proteins are ACE inhibitors that make koumiss a product that can be used as a component in anti-hypertensive functional products [10].

Influence on the immune system

A high percentage of nutrients, including vitamins and amino acids, contribute to immunomodulation, increasing the adaptogenic properties of the body. Valiev A demonstrated the effect of the essential fatty acids of mare's milk on immunocompetent cells and non-specific resistance after 6 weeks from the beginning of inclusion in the ration of mare's milk [11].

Secretory IgA is the main immunoglobulin of mare's milk. The homology of human secretory IgA and mare's was previously demonstrated by cross-reactions using human anti-IgA antiserum [12]. Corina Foekel et al in placebo-controlled studies with 23 patients demonstrated that the daily

intake of mare's milk with 250 ml for 16 weeks had a positive significant effect on the index of severity of atopic dermatitis decreased from 30.1 to 25.3 after 12 weeks of consumption ($P < 0.05$) (the Severity Scoring of Atopic Dermatitis -SCORAD) and fecal bifidobacteria increase from 4.6% to 11.9% ($P < 0.05$) [13].

The goal of the research of Spain and Polish scientists was to study the immune adaptations, the expression of congenital biomarkers and variations in the composition of the intestinal microbiota after the introduction of mare's milk in BALB/C mice that were sensitized intraperitoneally using β-lactoglobulin and α-casein in the skin with aluminum adjuvant. They measured IgE levels of serum antibodies and the expression of MCP-1, IL-4, and TNF-α in duodenum specimens. Changes in populations of immune cells in peripheral blood were quantified using flow cytometry and the composition of the intestinal microbiota was assessed using real-time PCR. The intake of mare's milk reduces serum IgE levels in sensitized mice. Groups that received mare's milk showed an increased population of regulatory T cells (CD4 + Foxp3 +). The mare's milk reduced IL-4 mRNA levels and led to higher TLR-4 transcripts in all treatment groups. However, the levels of MCP-1, TNF-α, and TLR-2 remained unchanged. After treatment, a positive effect was observed, with an increase in the number of intestinal Bifidobacterium spp. The immunomodulating properties of mare's milk were noted [1].

Functional parameters of phagocytosis were studied in 18 healthy volunteers taking 250 ml of mare milk, deep-frozen (FMM) or lyophilized (LMM) or cow milk (CM) daily for three weeks. Blood was taken before the intervention, weekly and then a week after the intervention. Chemotaxis of isolated polymorphonuclear leukocytes (PMN) was studied by means of a microporous filter analysis. Migration was determined fluorometrically. The activity of phagocytosis and a respiratory burst of PMN in whole blood was analyzed with Phago- and Bursttest® using flow cytometry. In contrast to the activity of phagocytosis, the chemotactic index (CI) and the activity of the burst significantly decreased in the FMM group. Immunostimulating effects attributed to the consumption of mare's milk were not observed in healthy volunteers, at least with respect to phagocytosis. The results of the study show that the use of FMM modulates inflammation processes, decreasing chemotaxis and respiratory burst, which may be beneficial for relieving inflammatory diseases [14].

Antiproliferative effect

Saumal and koumiss have an active therapeutic effect in a number of diseases such as tuberculosis and anemia. Regular consumption reduces the risk of developing cancer [15].

A. Guri and co-authors studied mare's milk for antimicrobial effect and antiproliferative properties [15]. In this study, raw mare's milk was reported to modulate the expression of the gene hilA and ssrB2 Salmonella typhimurium (qPCR) and has an antiproliferative effect on Caco-2 cells. The mare's milk, which has been heat treated, did not show a positive effect.

A number of scientists have studied the anticarcinogenic effect of molecules from milk of various origins [16-18]. Scientists Shariatikia et al. conducted a comparative study on cow, sheep, goat, mare, donkey, and camel milk, in addition to investigating the effect of their casein on

antiproliferative activity. According to the results, mare's milk casein has cytotoxicity against MCF7 cells (breast cancer cells). The results of the study suggested that there is a correlation between the anticancer activity of milk casein and their physicochemical properties such as the α-helix structure and the positive and negative charges of the protein that mare's milk casein possesses. Thus, mare's milk is a candidate for in vitro treatment of patients with cancer [19].

Influence of mare's milk on normal microflora

The mare's milk has a powerful detoxification effect. The mare's microflora neutralizes the effect of mutagens, possesses, replenishes with the necessary complex of nutrients and removes toxins from the body [13]. The milk has a certain degree of antimicrobial effect in relation to opportunistic and pathogenic fungi, bacteria, and viruses due to its own microflora.

Mare's milk is rich in active substances, natural enzymes that help the intestinal flora be regulated, limit the growth of unwanted bacteria, and improve the growth of bifidobacteria and lactic acid bacteria [13]. Furthermore, the composition of mare's milk provided immunoglobulins A, M, and G, which act as the markers of those microorganisms that can be pathogenic, which facilitates the protection task [3, 6, 13].

The high antimicrobial activity of mare's milk is associated with the lysozyme of [20], immunoglobulins, lactoperoxidase, and lactoferrin contained [21, 22]. Getting into the digestive tract lysozyme has a powerful normalizing effect on the composition of the microbial flora of the mouth and intestines. Lysozyme of breast milk is 100 times more active than lysozyme of cow's milk [21]. The growth of pathogenic flora was not only inhibited but the growth of bifidoflora was also promoted in the intestines of infants.

In addition to enzymatic activity, lysozyme possesses virucidal [23], immunostimulating [24], and fungicidal properties [25]. Lactoferrin in the composition of mare's milk supplements the antimicrobial effect [26]. The content of oligosaccharides is an excellent prebiotic factor for representatives of normal microbiota [26].

Antiallergic effect

The high homology of the mare's milk with human milk makes the product attractive for the development of baby food products, as well as functional products for the category with a pronounced allergic component [27]. A few years ago, the World Health Organization dubbed the new century the "age of allergy" and the disease itself as an "epidemic." According to WHO, from 2001 to 2010 the number of allergy sufferers in the world increased by 20% [27]. By 2025, WHO predicts 50% of the world population will suffer from this illness. According to the European Academy of Allergy and Clinical Immunology (EAACI), there are currently 150 million chronic allergic people in Europe (20% of the population). According to official statistics in the Republic of Kazakhstan, respiratory diseases are on the 1st place among all diseases in the Republic of Kazakhstan (2.5 million patients). About 1 million people suffer from bronchial asthma. The growth of allergic diseases is about 10-15% per year. Among them, the number increases with allergy to cow's milk.

Mare's milk was discovered to be the least reactive substitute, detected by both the enzyme-linked immunoassay (ELISA) and EAST method [27]. According to Curadi et al. (2001), mare's

milk is transferred to 96% of children with cow milk allergies [28]. Businco et al. investigated in vitro and in vivo allergenicity of mare's milk in 22 children aged 19 to 72 months. With appropriate changes, mare's milk can be considered as a good substitute for cow milk in most children with severe IgE-mediated cow milk allergy [29].

Fotschki J and co-authors conducted a series of studies on the analysis of immunoreactivity in mare's milk [1]. Fermentation of lactic acid was demonstrated to be significantly reduced the immunoreactivity of β-lactoglobulin, β-casein, κ-casein, and bovine serum albumin. The level of recovery was related to the type of bacterial strain: Lactobacillus casei LCY, Streptococcus thermophilus MK10, and Bifidobacterium animalis Bi30. The results of the study demonstrated that microbial fermentation with test strains is a valuable method of reducing the immunoreactivity of mare's milk proteins.

CONCLUSION

Despite the fairly well-illuminated material on the chemical composition of mare's milk, chemical and microbiological [30], experimental and clinical studies proving these or other positive effects on the body are not enough. This work reveals promising areas where mare's milk can be used for preventive purposes.

List of Abbreviations: FMM, frozen mare's milk; LMM, lyophilized mare's milk; CM, cow milk; PMN, polymorphonuclear leukocytes; CI, chemotactic index; qPCR, ssrB2 Salmonella typhimurium; EAACI, European Academy of Allergy and Clinical Immunology; ELISA, enzyme-linked immunoassay.

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