

WHEY PROTEINS - FACTS AND POSSIBILITIES IN MODERN MEDICINE

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ПРОТЕИНИ СУРУТКЕ – ЧИЊЕНИЦЕ И МОГУЋНОСТИ У САВРЕМЕНОЈ МЕДИЦИНИ

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ABSTRACT

The values of whey as a healthy and therapeutically useful drink are well known, and in folk medicine it has often been attributed miraculous powers and possibilities. This is nothing new, bearing in mind that in 460 BC, the father of medicine Hippocrates emphasized the value of whey in the treatment of tuberculosis, jaundice, diseases of the liver and digestive system, skin diseases and many other diseases. Whey is obtained during milk processing and cheese production, where it is present in almost 90% of the total mass. The composition of whey is specific. Water makes up to 93% of the composition, the rest consists of sugars and minerals, B vitamins, as well as a great wealth of probiotic bacteria. Whey is the largest source of essential amino acids compared to plant or animal sources. The concentration of amino acids in whey is 43% compared to oats (21%), wheat husk (21%) and wheat (22%), milk 39%, casein 34% and eggs 32%) or meat proteins (38%). Whey proteins contain almost 50% of essential amino acids and about 26% of branched-chain amino acids. Their composition is similar to the amino acid composition of human muscles, which allows their faster absorption than other sources of protein. The share of free amino acids in whey is 4 to 10 times higher than in milk. They have a significant effect on protein synthesis and a very strong anabolic effect in the body. Whey amino acids stimulate skeletal muscle regeneration, reduce fatigue, increase synthesis, and reduce muscle protein breakdown. Whey proteins increase the levels of antioxidant enzymes, especially glutathione and catalase. Positive effect on the reduction of the levels of TBARS (thiobarbituric acid reactive substance) is an important indicator of the decreasing process of lipid peroxidation. Reduction of oxidative stress process in the liver has positive consequences on inflammation and the content of lipids in the liver tissue and atherosclerosis process. Recent research indicates a positive effect on glucose metabolism, improving insulin sensitivity and preventing the development of fatty liver syndrome and type 2 diabetes. It has a positive effect on weight control, so whey proteins are integral parts of healthy medical diets, sport drinks, with approved efficacy in obesity treatments. Essential amino acids also act as neurogenic active

САЖЕТАК

Познате су вредности сурутке као здравог и терапијски корисног напитка, а у народној медицини њој се често приписују чудотворне моћи и могућности. То није ништа ново, имајући у виду да је 460. године пре нове ере Хипократ, отац медицине, истицао вредност сурутке у лечењу туберкулозе, жутице, болести јетре и органа за варење, кожних и многих других болести. Сурутка се добија прерадом млека и производњом сира, где је заступљена са скоро 90% укупне масе. Састав сурутке је специфичан. Вода чини до 93% састава, остатак чине шећери и минерали, витамини Б, као и велико богатство пробиотичких бактерија. Сурутка је највећи извор есенцијалних аминокиселина у поређењу са биљним или животињским изворима. Концентрација аминокиселина у сурутци је 43% у поређењу са зоби (21%), љуском пшенице (21%) и пшеницом (22%), млеком 39%, казеином 34% и јајима 32% или протеинима меса (38%). Протеини сурутке садрже скоро 50% есенцијалних аминокиселина и око 26% аминокиселина разгранатог ланца. Њихов састав је сличан саставу аминокиселина у људским мишићима, што омогућава бржу апсорпцију од других извора протеина. Удео слободних аминокиселина у сурутци је 4–10 пута већи него у млеку. Имају значајан утицај на синтезу протеина и веома јак анаболички ефекат у телу. Аминокиселине сурутке стимулишу регенерацију скелетних мишића, смањују умор, повећавају синтезу и смањују разградњу мишићних протеина. Протеини сурутке повећавају нивое антиоксидативних ензима, посебно глутатиона и каталазе. Позитиван ефекат на смањење нивоа ТБАРС (реактивна супстанца тиобарбитурне киселине) важан је показатељ опадајућег процеса пероксидације липида. Смањење процеса оксидативног стреса у јетри има позитивне последице на запаљење и садржај липида у ткиву јетре и процес атеросклерозе. Најновија истраживања указују на позитиван ефекат на метаболизам глукозе, побољшање инсулинске сензитивности и спречавање развоја синдрома масне јетре и дијабетеса типа 2. Позитиван је утицај на контролу телесне тежине, па су протеини сурутке саставни део здраве медицинске дијете, спортских напитака са доказаном ефикасношћу у лечењу гојазности. Есенцијалне аминокиселине делују и као неурогене активне

substances, and they are also known as precursors of biogenic amines and neurotransmitters, so it is logical that there is a growing interest in researching their potential in psychiatry.

Key words: whey; whey proteins; amino acids, essential; oxidative stress; diabetes mellitus.

INTRODUCTION

The values of whey as a healthy and therapeutically useful drink are well known, and in folk medicine it has often been attributed miraculous powers and possibilities. This is nothing new, bearing in mind that in 460 BC, the father of medicine Hippocrates, emphasized the value of whey as a therapeutic drink, confirmed by the fact that its use had a very invigorating effect on the body, so as such it was recommended in the treatment of tuberculosis, jaundice, skin diseases and similar diseases (1). Due to the richness of high-value proteins, these whey-based drinks are an ideal source of energy, building and nutrients for athletes, and there are more and more examples where they are an integral part of medical diets.

Whey production

Whey is a major by-product of the dairy industry. The main problem of the dairy industry is that only 10-20% of milk is used to obtain some of the products, while 80-90% of milk is whey (2). Whey is a liquid residue formed in the production of cheese and casein, formed as a consequence of the acid-enzymatic treatment of milk. Different ways of cheese production result in different forms of whey. Depending on the way milk is treated, different forms of whey are obtained, which can be sour, sweet, demineralized, with more or less lactose sugars and milk fats, and thus with different industrial or food uses. The amount of whey obtained during cheese production is almost equal to the amount of milk needed for its production, which means that during the production of 1 kg of cheese, about 10 liters of milk are consumed and thus an average of 9 kg of whey is produced, or 8-12 l of whey depending on the type of cheese produced (3). Due to its nutritional composition, whey is a very good substrate for use in various biotechnological processes, such as the production of microbial biomass and their metabolites. Nevertheless, only 50% of whey is used in the food and dairy industry, while the rest is discharged into watercourses without prior treatment (4, 5). Discharge of whey into watercourses causes major environmental problems due to the high values of chemical and biological oxygen demand and its negative impact on the biological world. Given that the estimate of world whey production is at the level of 200 million tons per year and with a tendency to grow, this amount of whey can be observed in two ways: as an excellent base for obtaining high quality energy building products in the diet, or as a

супстанце, а познате су и као прекурсори биогених амина и неуротрансмитера, па је логично да расте интересовање за истраживање њиховог потенцијала у психијатрији.

Кључне речи: сурутка, протеини сурутке, есенцијалне аминокиселине, оксидативни стрес, шећерна болест

potentially dangerous base for causing environmental problems in the natural environment (6).

Whey composition

According to the average composition, whey contains about 93% water, and over 50% of dry matter from milk is obtained from it. Most of whey is lactose, while less than 1% is whey protein (7). 70% of whey sugar is lactose and it is a very important energy source. Some of the beneficial effects of lactose are stimulating intestinal peristalsis, facilitating the absorption of calcium and phosphorus, establishing a slightly acidic reaction in the intestines, which prevents the growth and reproduction of harmful bacteria. The amount of mineral substances depends mainly on the method of its production, and the biggest variations are in the composition of calcium, phosphate, lactic acids and lactate, which are more present in sour whey than in sweet whey (8). The content of calcium and phosphorus is many times higher in sour whey, given that the higher the acidity of whey, the higher the solubility of minerals (Table 1)

In the richness of bacterial strains under whose influence various forms of lactic acids are developing, representatives of several important probiotic cultures (*Lactobacillus*, *Carnobacterium*, *Enterococcus*, *Leuconostoc*, *Oenococcus*, *Pediococcus*, *Tetragenococcus*, *Vagococcus*, *Lactococcus*, *Streptococcus* i *Weissella*) are included (9). Probiotic cultures, along with the genders of *Bifidobacterium* and *Lactobacillus*, are a significant source of bacterial cultures with a clear positive effect on the microbiota composition of intestinal contents and the impact on the immune and anti-inflammatory system of the intestine and the organism in general, especially given that these bacteria can produce lactic acid inside the lumen of intestines (10). Water-soluble vitamins also pass into whey from milk, but their content is variable. Whey may contain higher amounts of B vitamins, riboflavin, cobalamin, and folic acid, which are mainly bound to whey proteins, so in the production of cheese they are largely converted into whey. It is this increased amount of whey riboflavin that gives it its characteristic yellow-green color.

WHEY PROTEINS

Whey proteins are among the most nutritionally valuable proteins due to their composition, which is characterized by a large proportion of essential amino

acids. Due to this amino acid composition, whey proteins have a much higher biological value compared to casein or other protein sources. Essential amino acids cannot be synthesized in the body and therefore must be taken in through the diet. Essential amino acids from whey, especially leucine, are necessary to stimulate protein synthesis in muscle and represent a high proportion of amino acids that are necessary to stimulate muscle growth (11, 12). The utilization of whey protein in the body is closely related to the cystine / methionine ratio, which is about 10 times higher in whey protein than in casein (1). Free amino acids can be different in composition in whey, and their composition mostly depends on the degree of hydrolysis of casein in cheese production. Whey proteins are rich in branched chain amino acids such as isoleucine, leucine and valine. Unlike other essential amino acids, they are directly metabolized and transferred to muscle tissue where they are used to build / rebuild tissue during physical activity, exercise and fitness training (13). The contents of free amino acids in whey mostly depends on the degree of hydrolysis of casein (actions of enzymes and proteolytic acids of lactic acid bacteria), the process of technological processing and methods of production of different types of cheese (14). The share of free amino acids is therefore about 4 times higher in sweet whey than in milk, while in sour whey this share is up to 10 times higher, which is shown in Table 2 (15).

Whey is the largest source of essential amino acids compared to plant or animal sources. The concentration of these amino acids in whey is 43% compared to oats (21%), wheat shell (21%), wheat (22%), milk (39%), casein (34%), eggs (32%) or meat proteins. (38%) (16). This amount of possible amino acid intake enables the achievement of significant beneficial effects on protein synthesis and the achievement of a better anabolic effect in Table 1. Average chemical composition of sweet and sour whey (gr/l).

Ingredient	Sweet Whey	Sour Whey
Dry Matter	63-70	63-70
Lactose	46-52	44-46
Proteins	6.0-10.00	6.0-8.0
Calcium	0.4-0.6	1.2-1.6
Phosphates	1.0-3.0	2.0-4.5
Lactates	2	6.4
Chlorides	1.1	1.1

Table 2. Average chemical composition of sweet and sour whey (gr/l).

Ingredient	Free amino acids		In proteins	
	Total	Essential	Total	Essential
Whey				
Sweet	132.7	51	6.49	3.326
Sour	450.00	365.00	5.59	2.85

the body (17). The higher anabolic response is due to a greater increase in protein synthesis in the whole body and a significantly greater reduction in protein breakdown. The concentration of muscle proteins is significantly higher after consuming whey due to changes in protein synthesis throughout the body and this effect is dose dependent (18). Whey proteins contain 50% of essential amino acids and about 26% of branched-chain amino acids, and their composition is similar to the composition of human muscle amino acids, which allows faster absorption than other sources of protein. They stimulate skeletal muscle regeneration, reduce fatigue, increase synthesis and slightly reduce the breakdown of muscle proteins (18-20). This positive effect of whey amino acids on essential biomarkers in athletes (myoglobin and creatine kinase) is known and proven, helping athletes alleviate fatigue and reduce the risk of sport injuries, with easier crossing of the required aerobic threshold during physical activity (21).

Whey proteins - division into groups

Whey proteins have excellent functional properties such as good solubility, viscosity, gelling and emulsifying ability, so their concentrates are often used in the food industry. Because whey proteins are easier to digest than casein, they are also used in the production of infant food formulations, where it increases the nutritional value of the products. Whey proteins consist of immunoglobulins and other glycoproteins (lactoferrin, transferrin), enzymes (lysozyme, lactoperoxidase) and they are very important factors in preserving the immunoactivity potential. They have antimicrobial properties and can also reduce allergic reactions (22). Whey proteins also make up various thermolabile fractions such as β -lactoglobulins, α -lactalbumins, albumins, immunoglobulins, and the thermostable fraction of proteoses and peptones (1).

Whey proteins are divided into five main groups, plus additional smaller proteins due to different solubility, electrophoretic and chromatographic properties.

1. β -lactoglobulin (β -Lactoglobulin)- is the main protein of whey and makes up 40% of its proteins (23). It is a protein in bovine milk with more than 50% representation (24). It has a very important role in the body due to the ability to bind smaller molecules (vitamins, phospholipids, aromatic compounds) and thus facilitate their transport within the body. Binding molecules to this protein can alter their biological activities. These protein fractions have antihypertensive effects due to the possibility of inhibition of angiotensin-converting enzyme. Due to its ability to bind hydrophobic molecules, lactoglobulin has been used to improve the process of liposome encapsulation, and as such serves as a

useful auxiliary system for stabilizing vitamin E and curcumin in dietary products (25). This fraction of whey protein is a cheap and widely available antioxidant nutrient, which is otherwise responsible for more than 50% of the antioxidant activity of milk (26).

2. α -lactalbumin (α -Lactalbumin)- it differs from other proteins in solubility and makes up 20% of whey protein. It is rich in important amino acids - licine, leucine, cysteine and aspartic acid (27). In addition to its nutritional aspects, alpha-lactalbumin has been shown to have significant beneficial effects on child development. Alpha-lactalbumin can help bind minerals, induce apoptosis and suppress tumors, modulate the immune system, affect the intestinal microbiology of infants by promoting bifidobacterial strains and inhibiting the growth of potential pathogens.

3. Bovine serum albumin- contains 10% whey protein. It is not synthesized in the mammary glands and appears in milk after passive passage from the blood (28). Due to its size and structure, it can bind to fatty acids by participating in the synthesis of lipids (which are part of the outer and inner cells of the membrane). It also has an impact on energy production. It has antioxidant activity, thus protecting lipids from phenolic oxidation and strong inhibitory activity against the proliferation of breast cancer cells by modulating the activity of regulatory factors of autocrine growth (29).

4. Immunoglobulins are also known as "colostrum proteins" and make up about 10% of whey proteins. There are three main types of immunoglobulins: IgG, IgA and IgM. IgG is the dominant type of immunoglobulin in whey (30). Immunoglobulins ensure the proper and adequate functioning of antibodies (31). Immunoglobulins as well as lactoferrin are very rapidly enzymatically degraded in the gut and as such can be detected in target organs (brain, liver, intestines) in some 20 to 30 minutes after ingestion (32). These are easily digestible and useful protein structures with a proven positive effect on health (33). For these reasons, whey proteins, isolated lactoferrin or colostrum immunoglobulin proteins, are often used in athletes, during recovery after severe illness, to strengthen immunity, treat anemia. Supplementation of colostrum proteins, primarily immunoglobulin and lactoferrin, helps in the treatment of infections and respiratory allergies, as well as the processes of alleviating immunosuppression caused by intense exercise in athletes. Initial studies indicate that lactoferrin may be effective in combating SARS-COV 19 viruses, and that hyperimmune colostrum may be an alternative way to produce specific antibodies against COVID-19 (34), as it enhances the activities of the immune system at different levels of action: anti-inflammatory, antioxidant, and antiviral/antibacterial activity. Normally, more concrete conclusions on this issue require future larger, well-organized clinical studies, but preliminary research results are encouraging.

5. Proteases - (protease-peptone) are the most resistant whey proteins to temperature and make up 20% of all whey protein. Other proteins are present in whey in a lower percentage include lactoferrin, β 2 microglobuline (β 2 microglobulin) and glycoprotein.

- Lactoferrin is a multifunctional glycoprotein that binds to iron. It is important because of its antimicrobial properties and it aids in wound-healing processes (35). Recent research indicates its importance in controlling the immune response and in fighting infections of various origins.
- β 2 microglobulin appears in cow's milk by protease-dependent degradation of the cellular fraction of milk and has immunoregulatory properties. This protein is like certain parts of immunoglobulins (36).
- Glycoprotein is one of the smallest whey proteins.

WHEY PROTEIN – POSSIBLE HEALTH BENEFITS

Whey proteins, fulfilling their structure and amino acid composition, are very useful in human diet and have shown health effects. The positive benefits of their application are numerous. In recent research, the following stand out: high nutritional and biological value of amino acids, antioxidant activity, inhibition of angiotensin converting enzyme, potential anticarcinogenic effect, positive effect on weight control and satiety, possible antimicrobial effect, positive effect on bone metabolism and effect on osteoporosis prevention, providing sufficient amounts of vitamins B12, B6, B9, folic acid), a positive effect in the processes of wound growth and the creation of anti-inflammatory effects (37).

Whey proteins and their protective role during oxidative stress

Whey proteins are dominated by amino acids that are rich in cysteine and function as a donor system of cysteine in cells (38). Glutamine is important and it represents 4 to 5% of the total amino acid composition in our body. Glutathione is an important part of antioxidant cellular protection system and participates directly in this process, especially maintaining the value of ascorbic acid and tocopherols in the required active forms. Depletion of glutathione activity is a common consequence of increased free radical formation and occurs intensely in muscles during exercise. Glutathione has free radical scavenger properties with high levels of antioxidant activity (39). The use of whey protein has had a positive selective effect in the process of maintaining glutathione levels in healthy or cancer cells, thus representing a potentially useful modulator of cellular immune functions (40). Lymphocytic glutathione levels are increased by adding whey to the diet (41). It is known that an increase

in free radical levels leads to a decrease in glutathione levels (42). Whey proteins improve the protective antioxidant capacity against acute oxidative stress through multiple pathways. They maintain and strengthen the capacity of cells for survival, improve the activity of antioxidant protection enzymes; glutathione, catalase and sodium dismutase, and also have a positive effect on the process of inhibition of lipid peroxidation (43). The positive effect of whey protein on these enzyme systems is important due to the process of strengthening the body's general antioxidant protection, as well as through the process of protecting individual organs and their functions sensitive to changes in redox status (liver protection and better control of inflammatory processes) (44). Whey proteins increase basal metabolism and oxygen consumption in mitochondria and lower metabolic utilization of lipids in the diet due to lower negative energy impact of food, so these known effects are used in various diets (45). Whey protein supplements reduce lipid content in the liver, but only when they were the result of increased intake of cholesterol-rich foods (46). Whey proteins are a natural useful alternative to antioxidants, and their antioxidant activity is multiple, starting from whey proteins themselves, through specific mechanisms of action of fractions of other whey proteins (α -lactalbumin, β -lactoglobulin, bovine serum albumin and lactoferrin) (47-51). Whey proteins are a good source of sulfur amino acids because their sulfhydryl groups together with bioactive peptides are responsible for antioxidant activity (52). The use of whey peptides may increase the level of cellular glutathione and the activity of superoxide dismutase, important enzyme defense systems against free radicals, and there is evidence that di-hydrolyzed whey isolates can inhibit oxidative damage in the lungs (53).

Certain drugs have the potential to cause oxidative stress. The possibilities of controlling these negative effects of drugs while maintaining the positive therapeutic effects are very interesting. Treatment with olanzapine (an antipsychotic drug) has been associated with increased release of prooxidants and decreased activity of antioxidant markers (54). The addition of whey protein to the diet (alone or in combination with omega fatty acids) has managed to achieve partial positive control over the negative impact of measurable free radicals (54). Interestingly, these effects were better during the separate administration of whey protein from omega fatty acids, which indicates that at the level of dietary supplements there is the possibility of interactions and competition at the level of antioxidant enzymes, especially when given together with drugs (54). These forms of research are potentially interesting because they can examine the possibilities of beneficial synergism and antioxidant protection of the calf, during the application of many drugs.

Preventive use of whey protein in malnutrition conditions

With aging and reduced physical activity, loss of muscle mass can lead to negative health consequences. A good diet based on a controlled intake of adequate amounts of high-quality whey protein can help maintain the body's muscles, especially in combination with exercise (55). Whey proteins help maintain muscle tissue thanks to their composition and the presence of quality amino acids. These effects are useful in many ways for different profiles of users (older and younger people, recreationists, and athletes, during the process of maintaining body weight and controlling obesity). By maintaining an adequate body weight, the elderly can be protected from unwanted changes in body composition, as well as from many diseases that are usually associated with aging and obesity, such as heart disease, stroke, diabetes, and others. Older men after consuming whey protein showed a higher degree of protein synthesis as well as muscle growth, which helped to limit the loss of muscle mass and maintain good posture (56). Studies in elderly patients have shown the benefit of using whey protein in the treatment of sarcopenia, due to stimulation of postprandial protein synthesis and reduction of their loss (57).

Due to its positive nutritional effect, whey proteins in the form of dietary supplements have a potentially significant application in the treatment of malnutrition of various etiologies, including those that occur as a result of the development of malignant diseases. These patients are often on excretory treatment protocols (radiation or chemotherapy), which can lead to low nutritional status, most often due to nausea and lack of appetite (58). Normally, the use of whey protein in such conditions is required to be under the supervision of a physician.

Sports activities

During exercise and sports activities, protein synthesis decreases, so the need for their intake increases. The need for BCAA amino acids (branched-chain AAs - BCAAs) stands out. These amino acids have the ability to provide a quality source of energy during endurance training, so many athletes use them to ensure quality protein synthesis and muscle growth during the recovery period (59). Amino acid Leucine is a key BCAA factor in protein synthesis and has been found to play an important role in insulin and glucose metabolism. Whey proteins are particularly effective in stimulating the rate of muscle protein synthesis because whey protein composition is very similar in profile of skeletal muscle (60). Therefore, whey protein is considered the "gold standard" in the diet of athletes, which is understandable, given that their need for protein intake is up to twice the usual needs (61).

Obesity, cardiometabolic diseases, diabetes

Increased plasma concentrations of some gastrointestinal hormones are associated with a feeling of satiety after the administration of whey protein. The use of whey amino acids and their metabolites can have a positive effect in controlling the hunger / satiety response. Whey protein in female subjects showed a positive effect on gastrointestinal hormones associated with satiety. Decreases in ghrelin, increases in cholecystokinin, glucagon-like peptides (GLP 1), peptide tyrosine and pancreatic polypeptides, increases in total amino acid concentrations, increases in plasma urea and ammonia, were observed after whey protein intake and were associated with weight loss and increased satiety feeling in the respondents (62). A high-protein diet can reduce body weight and increase insulin sensitivity. Whey protein intake in concentrate in insulin-resistant experimental animals reduces tissue lipid levels and body fat percentage, reduces body weight by 4%, reduces plasma insulin concentration by 40% and increases insulin sensitivity compared to a protein-rich diet of red meat (63). Weight loss under energy restriction is associated with high levels of calcium and whey protein in the diet (64). In experimental animals, that were fed high-calorie fatty foods with high calcium content, the use of whey protein was able to inhibit the accumulation of body fat. They acted on changes in adipocyte gene expression and leptin signaling regulatory pathway, as well as increasing adrenergic signaling pathway activity via the $\beta 3$ adrenergic receptor (65). High doses of calcium in the diet inhibit the synthesis of bioactive vitamin D. Inhibition of calcium levels in adipocytes reduces lipogenesis and promotes lipolysis, which is one of the mechanisms of the influence of whey protein on the weight loss process. Whey protein in a high-fat meal has excellent effects on postprandial triglyceride levels (values after a high-fat meal) in patients with type 2 diabetes (66). A diet based on increased intake of high-energy foods in combination with a physically insufficiently active lifestyle significantly contributes to early insulin resistance, increased blood lipid levels and hepatic steatosis, known as early predictors of type 2 diabetes, non-alcoholic fatty liver and consequent metabolic syndrome. One in three patients with nonalcoholic fatty liver disease has diabetes, and approximately three to four patients with type 2 diabetes have some form of fatty liver disease (67). The connection between fatty liver syndrome and diabetes exists and is visible on pathohistological examinations of the liver in experimental animals with diabetes and non-alcoholic fatty liver, in which liver damage by steatosis is visible, which is confirmed by biochemical parameters (68). There is a greater improvement in insulin sensitivity and reduction in resistance to it, after the use of whey protein in the form of dietary supplements, so their use may be

useful in slowing the development of fatty liver disease and type 2 diabetes (69).

The use of whey protein can further reduce the risk of hypertension and cardiovascular disease. Positive antihypertensive activity, defined by inhibition of angiotensin-converting ACE enzyme, has been confirmed for several peptides derived from milk protein proteolysis (70). β -lactoglobulin (β -Lactoglobulin) exerts its antihypertensive effect together with a positive effect on lowering cholesterol (71). Non-hydrolyzed β -lactoglobulin has very low ACE inhibitory activity, but its hydrolysis (using pepsin, trypsin, chymotrypsin and / or other proteases) has resulted in high values of ACE enzyme inhibition (73% -90%) and potential antihypertensive activity (72). Preventive use of whey protein in the form of dietary supplements can be useful for patients who have an increased risk of cardiovascular disease, but also as a good dietary support during therapeutic procedures in the treatment of hypertension and its consequences.

Psychiatric diseases

Biogenic amines such as norepinephrine, serotonin, dopamine, and histamine are synthesized from their precursors, tryptophan, tyrosine, and histidine. The values of these precursors amino acids in the central nervous system depend on the concentration of the amino acids phenylalanine, valine-leucine and isoleucine in the blood and the affinity of tyrosine and tryptophan carriers to allow them to cross the blood-brain barrier (73, 74). The amino acids serine, glycine, aspartic and glutamic acid act as neurotransmitters and help in the development of neurons, so imbalances of these levels of neurotransmitters have been recorded in patients with schizophrenia (75). Changes in the concentration of these amino acids in plasma may increase the possibility of psychotic disorders and may have an impact on the outcome of treatment. Therefore, it should come as no surprise that there is an increased interest in discovering the possible role of amino acids in the pathophysiology of schizophrenia, with an evident focus on glutamate and gamma amino butyric acid (GABA) (76).

In schizophrenic patients, oxidative stress has been recognized as a possible causal mechanism of the disease and complicating its clinical development, due to the imbalance between the production of free radical reactive oxygen and nitrogen species and the levels of available antioxidant defense systems (77). This process is complicated by the further development of pathophysiological mechanisms such as mitochondrial dysfunction, inflammation, lipid peroxidation, DNA damage and the development of apoptosis (78). The use of certain antioxidants such as N-acetyl cysteine, alpha lipoic acid, melatonin, essential amino acids, increases the level

of glutathione in plasma in patients with schizophrenia (79). Hypofunction of the NMDA receptor (N-methyl-D-aspartate (NMDA)) for glutamate is one of the theories of schizophrenia development and possible mechanisms of complications of the pathophysiology of the disease (80, 81). Therapeutic use of certain amino acids can affect the functionality of NMDA receptors and lead to improved symptoms of schizophrenia. Glycine, D-cycloserine, D-serine, act as co-agonists at the NMDA receptor and may lead to improvement of negative symptoms in patients with schizophrenia (82). Whey proteins are an excellent source of these useful amino acids, so it is logical that there is a growing interest in researching their potential in psychiatry.

COMMERCIAL STATUS OF WHEY PROTEIN-BASED PRODUCTS

A wide range of whey protein products is available in markets around the world. The most common available forms of whey protein are concentrates (whey protein concentrate), isolates (whey protein isolates), hydrolyzed whey protein concentrates (hydrolyzed whey protein concentrate) and hydrolyzed whey protein isolates (hydrolyzed whey protein isolate) (83). Some manufacturers of infant feed formulas increase the amount of whey protein in their products by increasing the percentage of total protein (increase in lactoferrin and alpha-lactalbumin), which brings their composition closer to the properties of breast milk and their better utilization. The application of different forms of whey protein and their composition are shown in Table 3.

CONCLUSION

Whey proteins are an excellent source of high-nutrient and low-calorie substances necessary for the normal functioning of living beings. Essential amino acids and different whey protein fractions are increasingly the focus of research and broader definitions of their health benefits. They play an important role in the prevention and assistance in the treatment of various health conditions. They are indispensable ingredients in the production of food for infants and young children, they help in recovery from effort and achieve better performance and results obtained by athletes and recreationists. Their clear influence on immunity (especially certain protein fractions) opens new chapters in research on the problem of the immune response to various infections and allergic conditions. The essential amino acids of whey are a significant precursor to important neurotransmitter processes in the nervous system, and it is a logical interest of researchers to use them in the prevention and treatment of neuropsychiatric diseases. The high degree of antioxidant protection of the organism by whey proteins, especially certain protein fractions, give whey proteins a different, positive dimension of the control of oxidative stress and its consequences. The low-calorie value of whey protein is a good choice in creating balanced diets for weight loss, with particularly significant effects on the development of negative cardiometabolic consequences of metabolic syndrome with or without diabetes. This effect is all the more important, having in mind the shown positive effects on hypertension, non-alcoholic fatty liver disease and diabetes, which have been confirmed by

Table 3. Overview of the most common commercial whey products and their application

Product	Proteins	Lactose	Fats	Application
Whey powder	11-14.5%	63-75%	1-1.5%	It is most often used in the food industry, bakery products
Whey proteins - concentrates	25-89%	4-52%	1-9%	The most common commercial form of whey protein. They are used in the production of protein drinks and meals, in the bakery industry, the dairy industry (yogurts, creams, ...)
Whey proteins - isolates	90-95%	0.5-1%	0,5-1%	Protein supplementation in cases of malnutrition and additional needs of the body for protein, protein meals and supplements, sports nutrition
Whey proteins - hydrolyzed concentrates	More than 80%	Less than 8%	Less than 10%	Sports drinks
Whey proteins - hydrolyzed isolates	More than 90%	0.5-1%	0.5-1%	They contain easily digestible peptides that reduce the risk of allergies reaction in sensitive individuals. They are usually used in adapted formulas for infants and athlete's diet.

adequate study analyzes. The turnover of products based on whey proteins is increasing every day. Wide possibilities of application and diversity of forms and composition, enable manufacturers to present and advertise these products through various channels of communication with users. Given the specificity and potential positive benefits of using whey protein in the prevention and maintenance of health, but increasingly in helping to treat certain diseases and conditions, it is clear that there is a need for increasing control and supervision by experts during recommendations and implementation of these products. The positive effects of whey protein on the heart, cardiovascular system and glucose metabolism have been identified as promising, but require additional, larger and better organized research, in order for these products to become part of important therapeutic recommendations. With the further development of technology, high-quality and purified whey protein fractions will be obtained, so this important and important nutritious food will gain increasing importance in the prevention and help in the treatment of various diseases and conditions.

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