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HEALTH-PROMOTING PROPERTIES OF SELECTED MILK COMPONENTS

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Abstract

The human diet should be a rich source of nutrients, energy and tissue-building materials. Bovine milk is one of the few food products of animal origin that meet the above requirements. It contains proteins rich in readily available amino acids, fatty acids, vitamins, micronutrients and macronutrients, such as calcium, magnesium, phosphorus, sodium, iodine, potassium, chlorine and small quantities of iron.

This study discusses the positive effects of bovine milk on human health, resulting from its composition and high nutritive value. We have reviewed numerous publications and reports indicating that milk contains readily available amino acids, unsaturated fatty acids which are vital components of the human diet, as well as macronutrients and micronutrients that regulate biochemical processes in the body. Particular attention has been paid to the anti-carcinogenic, antioxidant, anti-sclerotic, anti-inflammatory and antibacterial properties of milk, which is also known to lower blood pressure and strengthen the immune system.

The health benefits delivered by selected minerals contained in milk are also described. Calcium content largely determines the nutritional value and heat stability of milk, as well as its suitability for cheese production. Milk calcium is easily absorbed, and it is characterized by a high level of physiological activity due to a favorable calcium to phosphorus ratio of 1.2:1. Milk contains 0.75 g-1.10 g dm^{-3} of phosphorus, and phosphorus concentrations are generally stable and independent of the nutritional regime of cows. The magnesium content of milk is determined in the range of 100 to 150 mg dm^{-3}. In milk, magnesium is found in the form of soluble compounds (75% of total Mg) as well as colloidal compounds (phosphates, citrates). Magnesium concentrations are correlated with the calcium content of milk. The magnesium to calcium ratio determine milk's heat stability. Milk contains 1.35 to 1.55 g dm^{-3} of fully ionized potassium. The sodium content of milk is

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determined at 350-600 mg dm^{-3}, and chlorine levels are noted in the range of 0.80-1.40 g dm^{-3}. Sodium chloride stabilizes the osmotic pressure of milk (including lactose). Milk contains trace quantities of iron (0.42 to 0.45 mg kg^{-1}).

Key words: milk, proteins, fatty acids, macronutrients, micronutrients, amino acids, human diet.

PROZDROWOTNA WARTOŚĆ WYBRANYCH SKŁADNIKÓW MLEKA

Abstrakt

Dieta człowieka powinna zawierać produkty bogate w składniki odżywcze, budulcowe i energetyczne. Jednym z nielicznych surowców pochodzenia zwierzęcego spełniającym wymienione warunki jest mleko krowie. W swoim składzie zawiera białka bogate w łatwo przyswajalne aminokwasy, kwasy tłuszczowe, witaminy oraz mikro- i makroelementy, takie jak wapń, magnez, fosfor, sód, jod, potas, chlor oraz w niedużej ilości żelazo.

Celem pracy było wykazanie wartości odżywczej mleka w aspekcie jego bogatego składu i pozytywnego wpływu na zdrowie człowieka. Na bazie literatury wykazano, że mleko zawierając łatwo przyswajalne aminokwasy, niezbędne dla człowieka nienasycone kwasy tłuszczowe oraz makro- i mikroelementy pozytywnie wpływa na wiele przemian biochemicznych w organizmie. Zwrócono szczególną uwagę na udokumentowanie właściwości antynowotworowych, antyoksydacyjnych i przeciwmiażdżycowych mleka, a także działanie przeciwzapalne, antybakteryjne, obniżające ciśnienie krwi i wzmacniające układ odpornościowy.

W pracy podano także znaczenie dla zdrowia człowieka wybranych pierwiastków, tj. wapnia, fosforu, magnezu i żelaza. Podano, że wapń decyduje o wartości odżywczej mleka, jego stabilności cieplnej i przydatności do produkcji serów. Jednocześnie wykazano, że charakteryzuje się dobrą przyswajalnością i aktywnością fizjologiczną ze względu na korzystny dla organizmu człowieka stosunek do fosforu, wynoszący 1,2:1. Ponadto ukazano zawartość w mleku niektórych pierwiastków w kontekście aspektów warunkujących te zależności. Określono, że poziom fosforu w mleku jest stały i niezależny od żywienia, w granicach 0,75-1,10 g dm^{-3}. Zawartość magnezu w mleku wynosi od 100 do 150 mg dm^{-3}. Pierwiastek ten występuje w formie związków rozpuszczalnych (75% ogólnej ilości Mg) oraz koloidalnej (fosforany, cytryniany). Ilość magnezu jest skorelowana z ilością wapnia w mleku. Stosunek ten decyduje o stabilności cieplnej mleka. Zawartość potasu w mleku waha się od 1,35 do 1,55 g dm^{-3} w formie całkowicie zjonizowanej. Zawartość sodu w mleku wynosi 350-600 mg dm^{-3}, a chloru 0,80-1,40 dm^{-3}. Rola chlorku sodowego polega na utrzymaniu ciśnienia osmotycznego mleka (wraz z laktozą) na stałym poziomie. Mleko zawiera niewiele żelaza (od 0,42 do 0,45 mg kg^{-1}).

Słowa kluczowe: mleko, białka, kwasy tłuszczowe, makroelementy, mikroelementy, aminokwasy, dieta człowieka.

INTRODUCTION

According to current scientific knowledge, the human diet should incorporate around 60 nutrients that are essential for growth, development and functioning of the body. Human breast milk and bovine milk are nutritionally the richest foods of animal origin (Przybojewska, Rafalski 2003). For adult

humans, milk and dairy products are a vital source of energy, tissue-building nutrients and components that play a regulatory role in the body (SÉVERIN, WENSHUI 2005). As demonstrated by research studies, the bioactive components found in milk prevent obesity and cancer, and they offer a variety of health benefits for consumers (PARODI 1997, BARR 2003, ZEMEL 2003). Humans are quite special in this respect as no other mammals consume milk regularly after reaching adulthood (ARAKAWA et al. 1999).

The biological value of milk is determined by the content of bioactive components that offer health benefits (REKLEWSKA et al. 2005, WONG et al. 2006). Recent years have witnessed a growing interest in functional foods, including milk (WARD, GERMAN 2004). Milk contains biologically active substances, including proteins, peptides, amino acids, sugars, vitamins, enzymes, sterols, phospholipids and fatty acids which regulate biochemical processes in the human body. Milk is also a source of polyunsaturated fatty acids (PUFA), which have anti-carcinogenic, antioxidant, anti-sclerotic, anti-inflammatory and antibacterial properties. PUFAs effectively lower blood pressure and reinforce the immune system (BARŁOWSKA et al. 2005, STANTON et al. 2005, KRÓL et al. 2006, WONG et al. 2006).

Milk provides a plethora of bioactive ingredients for incorporation into functional food products. This has come at a time when consumers want more from food than just basic nutrition, including the prevention of lifestyle diseases through a healthy diet. Using milk as a model system could prove invaluable for developing designer foods or even 'designer milk', a concept that has been discussed in a review by SABIKHI (2007). However, it should be noted that many of the physiological effects observed for the bioactive components of milk have only been proven *in vitro* or in animal models and have yet to be proven in humans. Another major challenge faced by food scientists and manufacturers alike is the cost-effective large-scale production of milk bioactive ingredients. For example, while the potential for milk proteins and peptides as ingredients in functional food products has been well documented on a vast scale, their large-scale production and commercialization are still limited. Major efforts are now underway to develop methods to ensure optimal activity of these agents in food systems and their subsequent utilization in the body. One group has recently cloned the 11-residue antimicrobial peptide from bovine lactoferrin (BL-11) and the 12-residue hypotensive peptide from αs1-casein (C-12) in the dairy starter culture *Streptococcus thermophilus*, which is utilized in the production of yoghurt and various cheeses (RENYE, SOMKUTI 2008). Multiple repeats of the hypocholesterolemic peptide IIAEK, derived from bovine milk β-lactoglobulin, have been introduced into the five variable regions of soybean proglycinin A1aB1b and when expressed in *E. coli* have demonstrated the large-scale production of a small peptide of fewer than 10 amino acids (PRAK et al. 2006, PRAK, UTSUMI, 2009). The potent antihypertensive peptide derived from ovalbumin, RPLKPW (novokinin), has recently been incorporated into the soybean through transgenesis (YAMADA et al. 2008). Through such appro-

aches, milk bioactive peptide sequences may even be incorporated into food proteins of non-dairy origin. However, using molecular genetic approaches to increase the bioavailability or production of therapeutic peptides is perhaps an unrealistic goal, considering the strict regulations governing the use of genetically modified organisms in the food industry in certain parts of the world. The existing modern technologies applicable for the isolation of bioactive native proteins and peptides from milk are beyond the scope of this review but have been discussed in detail by KORHONEN and PIHLANTO (2003, 2007).

This study discusses the nutritive value and the positive health effects of bovine milk based on a review of scientific evidence.

Milk tolerance

Most consumers tolerate milk and its nutritional components, but some adult humans are unable to digest milk due to lactose intolerance. This defect results from an absence of lactase, an enzyme produced by the small intestine which hydrolyzes lactose into glucose and galactose. Nearly 70% of the worldwide population is lactose intolerant. The above applies to approximately 5% Caucasians, whereas other ethnic groups are much more severely affected (around 90% Chinese adults, 85% Aboriginal Australians, more than 45% indigenous Africans). In Poland, lactose intolerance affects 1.5% infants and children and 20-25% adults. The latest population research advocates the production of lactose-free milk and recommends that lactose-intolerant people should limit their milk consumption (JACKSON, SAVAIANO 2001, KEITH et al. 2011).

Nutritional value of milk

Milk is one of the most nutritionally complete foods in the human diet. Its high nutritive value can be attributed to its unique chemical composition which supports optimal digestion and absorption. The nutritional value of milk is determined by its energy value, digestibility, assimilability and biological properties. Milk dry matter contains nutrients that are vital for the growth and healthy functioning of the human body: lactose, protein, fat, minerals and vitamins. The energy content of milk is a sum of individual energy contributing components – 49% fat, 40% milk sugar and 11% proteins. The composition of milk varies subject to the breed of dairy cows, their nutritional regime, successive lactation, lactation stage, season and herd management practices (WALSTRA et al. 1999).

Proteins and peptides

The nutritive value and processing suitability of milk are determined mainly by its protein content. The major protein fractions in milk are casein and whey proteins, including immunoglobulins, α-lactalbumin, β-lactoglobulin, lactoferrin and transferrin (SEVERIN, WENSHUI 2005) – Table 1.

Table 1

Concentration and biological activity of major bovine milk proteins (Séverin, Wenshui 2005, Walstra, Jenness 1984, Yamauchi 1992, Korhonen et al. 1998)

Protein	Concentration (g L^{-1})	Function
Total caseins	26.0	ion carrier (ca, po4, fe, zn, cu), precursor of bioactive peptides
α-casein	13.0	precursor of bioactive peptides
β-casein	9.3	precursor of bioactive peptides
κ-casein	3.3	precursor of bioactive peptides
Total whey protein	6.3	anti-carcinogenic, weight management
β-Lactoglobulin	3.2	retinol carrier, binding fatty acids, possible antioxidant
α-Lactalbumin	1.2	lactose synthesis in mammary gland, ca carrier, immunomodulation
Immunoglobulins (A, M, and G)	0.7	immune protection
Serum albumin	0.4	
Lactoferrin	0.1	antimicrobial, antioxidant, immunomodulation, iron absorption
Lactoperoxidase	0.003	antimicrobial
Lysozyme	0.0004	antimicrobial, synergistic effect with immunoglobulins and lactoferrin
Miscellaneous	0.8	
Proteoseepeptone	1.2	function unknown; precursor of bioactive protein and peptide in vitro
Glycomacropeptide	1.2	antiviral, bifidogenic

Milk proteins contain a full range of exogenous amino acids, whose concentrations exceed the recommended daily protein intake for adults formulated by the Food and Agriculture Organization of the United Nations (FAO) in 1990. The protein content of milk varies from 2.6% to 5.3%, depending on genetic and environmental factors (Miciński et al. 2008). Protein levels in milk largely determine cheese yield per 100 kg of milk. Casein accounts for 78% of all milk proteins, and the casein content of milk ranges from 2.2% to 3.6% (Grega 1999). There are five main casein fractions: αs1-casein, αs2-casein, β-casein, γ-casein, and κ-casein (Pikul 2004). Bovine milk proteins are also functional food components that deliver nutritional and health benefits (Pikul 2004). In the group of six milk protein fractions, two polymorphic forms, β-lactoglobulin and κ-casein, are genetic markers for quantitative trait loci which determine the chemical composition of milk and cheese yield (Aleandri et al. 1990, Litwińczuk et al. 2006).

Milk also contains whey proteins, including β-lactoglobulin (2-4 g dm^{-3}) and α-lactalbumin (1.0-1.5 g dm^{-3}) (MICHALSKI, JANUEL 2006). They are a rich source of lysine, methionine and cysteine, as well as essential amino acids such as threonine and tryptophan. All bovine milk proteins, including casein, are an abundant source of lysine, an essential amino acid which is found in very small quantities in cereals. The consumption of milk, hard cheese or cottage cheese with bread supplements lysine-deficient wheat proteins with this essential amino acid. As a result, cereal proteins become wholesome building blocks that are absorbed by the body and used to build new tissue (ZMARLICKI 2006). Whey amino acids are commonly used in the production of food supplements for athletes, elderly consumers and recovering patients. As foreign antigens, bovine milk proteins may cause an allergic reaction in humans (ZWIERZCHOWSKI et al. 2011). Their anti-mutagenic and anti-carcinogenic properties have been demonstrated in an *in vitro* study (ZMARLICKI 2006).

The medicinal properties and uses of milk proteins have been extensively studied (MADUREIRA et al. 2007, ZIMECKI, KRUZEL 2007). Research results show that whey, containing lactoferrin, β-lactoglobulin and serum albumin, contributes to suppressing the growth of neoplastic cells (PARODI 2007) and accelerates their apoptosis (SVANBORG et al. 2003). The utilization of whey as a functional food ingredient for weight management is attracting much interest (LUHOVYY et al. 2007). The special membrane structure surrounding milk micro-lipid droplets, composed of a lipid bilayer and proteins, termed the milk fat globule membrane (MFGM), has also shown potential as a therapeutic agent against many pathological conditions (SPITSBERG 2005). One of the proteins isolated from MFGM, referred to as the fatty acid binding protein (FABP), has been shown to inhibit some breast cancer cell lines (SPITSBERG, GOREWIT 1997a, 2002). In addition, the onco-suppressor protein BRCA1 has also been found in both bovine and human MFGM (SPITSBERG, GOREWIT 1997b). WANG et al. (2001) also demonstrated that glycoproteins of MFGM were capable of inhibiting the infection of *Helicobacter pylori* in a BALB/cA mouse model, and the hemagglutination and adhesion of *Helicobacter pylori* in HeLa S3 monolayers.

Bioactive peptides which exert numerous physiological responses can also be generated from milk proteins in the gastrointestinal tract. Such bioactive peptides are latent or encrypted within native protein precursors, thus proteolysis is required for their release (GOBBETTI et al. 2004). Bioactive peptides have been generated from most of the major proteins in both bovine and human milk (SÉVERIN, WENSHUI 2005). Bioactive milk peptides were first described in 1950, when MELLANDER (1950) reported that ingestion of casein-derived phosphorylated peptides led to enhanced vitamin D-independent calcification in rachitic infants. While bioactive peptides can be generated from a variety of foods, milk proteins are generally regarded as a very rich source of those peptides and, as a result, have become fundamental constituents of several commercially available functional food products and ingredients (Table 2).

Table 2

Compositions and concentrations of oligosaccharides in bovine milk, bovine colostrum and human milk (Mehr, Kelly 2006, Kunz, Rudloff 200), Gopal, Gill 2000, Nakamura, Urashima 2004

Oligosaccharide	Bovine milk (g L^{-1})	Bovine colostrum (g L^{-1})	Human milk (g L^{-1})
Lactose	40 - 50	40 - 50	55 - 70
Neutral oligosaccharides			
Lacto-N-tetraose	trace	-	0.5 - 1.5
Lacto-N-fucopentaose I	-	-	1.2 - 1.5
Lacto-N-fucopentaose II	-	-	0.3 - 1.0
Lacto-N-fucopentaose III	-	-	0.01 - 0.2
Lacto-N-difucohexaose I	-	-	0.1 - 0.2
Lacto-N-novopentaose		NR*	
N-acetylgalactosaminylglucose		NR*	
N-acetylgalactosyl-lactose		NR*	
α-3'-galactosyl-lactose		NR*	
β-3'-galactosyl-lactose		NR*	
6'-galactosyl-lactose		NR*	
N-acetyl-lactoseamine		NR*	
N-acetyl-galactosaminyl-lactose			
NeuAc(a2e6)lactose	0.03 - 0.06	0.019	0.3 - 0.5
NeuAc(a2e3)lactose		0.095	0.1 - 0.3
N-glycoylneuraminyl-lactose			
NeuAc-lacto-N-tetraose a	trace	-	0.03 - 0.2
NeuAc-lacto-N-tetraose c	trace	-	0.1 - 0.6
NeuAc2-lacto-N-tetraose	trace	-	0.2 - 0.6
6-Sialyl-lactosamine		0.047	
3-Sialyl-galactosyl-lactose		trace (3 µmol L^{-1})	
Disialyl-lactose		0.028	
Sialyl-lactose-1-phosphate		trace (3 µmol L^{-1})	
Sialyl-lactose-6-phosphate		trace (1 µmol L^{-1})	
3-Glycolyl-neuraminyl-lactose		trace (2 µmol L^{-1})	
6-Glycolyl-neuraminyl-lactose		NR	
GlcNAcb(1-3)Galb(1-4)	-	-	-
GlcNAcb(1-3)Galb(1-4)Glc	-	-	-

* NR – oligosaccharides detected and structurally characterized, but concentration not reported

Bioactive peptides from milk can be divided into the following categories based on their physiological effect on the body or the protein from which they have been derived: antihypertensive, antithrombotic, opioid, casein phosphopeptides (CPPs), antimicrobial, cytomodulatory, immunomodulatory, and miscellaneous peptides (HAYES et al. 2007).

Antithrombotic peptides that interfere with the formation of thrombi have also been identified in milk (ZIMECKI, KRUZEL 2007). Enzymatic hydrolysis of κ-casein has resulted in some of the most antithrombotic peptides to date from food sources. Thrombosis is a pathological condition that results in clot or thrombus formation in arteries, veins or the ventricles of the heart. It is interesting that comparisons can be drawn between the mechanisms involved in milk clotting, defined by the interaction of κ-casein with chymosin. and the mechanisms of blood clotting, defined by the interaction of fibrinogen with thrombin (RUTHERFURD, GILL 2000).

The so-called opioid peptides can also be found in bovine milk**.** Opioid peptides show pharmacological similarities to opium. Caseins (αs1-, αs2,- β- and κ-) and whey proteins are potential sources of opioid peptides. However, the major opioid peptides are fragments of β-casein, called β-casomorphins (CLARE, SWAISGOOD 2000). Similar proteins have also been reported from human β-casein fractions. On the other hand, all κ-casein fragments, known as casoxins, behave as opioid antagonists (SÉVERIN, WENSHUI 2005). Opioid peptides have also been found encrypted within the primary sequence of whey proteins such as lactoferrin, β-lactoglobulin, and bovine serum albumin (BELEM et al. 1999). β-casomorphins are resistant to the action of gastrointestinal enzymes and have been associated with the following activities: antihypertensive, immunomodulatory, antidepressant, anti-secretory and anti-diarrheal (PIHLANTO 2001). Opioid peptides are thought to be biologically very potent; potentially, micromolar amounts may be sufficient to exert physiological effects (MEISEL, FITZGERALD 2000).

Milk is a rich source of antimicrobial proteins and peptides, capable of exerting antimicrobial activities comparable to antibiotics. This effect is due to the synergistic activity of naturally occurring peptides and defense proteins besides immunoglobulins, such as lactoferrin, lactoperoxidase and lysozyme and is greater than any individual contribution (CLARE et al. 2003, SÉVERIN, WENSHUI 2005). The potent properties of these agents can be reflected by the example of bovine lactoferrin, which has displayed strong antiviral activity against HIV and the human cytomegalovirus, the latter of which is thought to act synergistically in patients with acquired immunodeficiency syndrome (FLORIS et al. 2003).

Milk fat

Milk fat is a concentrated source of energy (48% of the total energy value of milk), responsible for the pleasant flavor of milk. Owing to its high digestibility and nutritional value (up to 99%), bovine milk fat plays an im-

portant role in human nutrition, although its fatty acid profile is less than ideal (Barłowska, Litwińczuk 2009).

Fat is not a homogenous substance, and it comprises fat globules which are dispersed in the aqueous phase of milk to form an emulsion. Fat globules contain triacylglycerols that account for 98% of milk fat. Their membrane consists of glycoproteins, 1.1% phospholipids, monoacylglycerols (0.16--0.38%), diacylglycerols (0.28-0.59%), free fatty acids (0.1-0.4%), sterols (0.42%), carotenoids and fat-soluble vitamins (Górska et al. 2006).

Bovine milk fat is characterized by one of the most complex structures among all natural fats. According to various authors, it contains from 400 (Jensen 2002) to around 500 fatty acids (Reklewska, Bernatowicz 2003), of which only 15 have more than a 1% share of the total fat content, but their combined composition (by weight) accounts for approximately 95% of the total fatty acid profile. Around 36 fatty acids and their isomers have more than a 0.1% share of the fatty acids profile in milk. The remaining fatty acids are found in trace quantities (Parodi 2004).

Fatty acids – functional components of milk, whose properties are determined by the length of the hydrocarbon chain and the number of unsaturated bonds, have a decisive impact on fat quality. They are synthesized by ruminal microflora from acetate, β-hydrobutyrate, triacylglycerols, lipoproteins and, in smaller quantities, from sterols, phospholipids and free fatty acids. The nutritive value of milk is also determined by the presence of minerals essential for human health (Bodkowski et al. 2004, Parodi 2004, Barłowska et al. 2005).

Fatty acids which are chain compounds with 4 to 16 carbon atoms are synthesized by the glandular tissue of the udder, whereas fatty acids with a longer chain are produced in the blood plasma. The diet of dairy cows can by manipulated to affect the content of milk fat (Barłowska, Litwińczuk 2009).

Bovine milk contains approximately 70% saturated fatty acids and 30% unsaturated fatty acids. The latter are composed of monounsaturated fatty acids (MUFAs) in around 83% and polyunsaturated fatty acids in 17% (Brzóska et al. 1999).

The unique value of bovine milk fat can be attributed to short-chain and medium-chain fatty acids (14% share of total fatty acids), which provide a source of energy for muscles, heart, liver, kidneys, blood platelets and the nervous system. The above fatty acids do not increase blood lipid levels and they do not contribute to the risk of obesity (Barłowska, Litwińczuk 2009). Butyric acid plays an important role in the prevention and treatment of colorectal cancer. It stilts the development of neoplastic cells by inhibiting DNA synthesis in their nuclei. Short-chain fatty acids contribute to the treatment of colorectal diseases, including inflammatory bowel disease and ulcerative colitis (Przybojewska, Rafalski 2003).

Long-chain fatty acids contain 16 and more carbon atoms, and they have an estimated 56-68% share of the total fatty acid profile in bovine milk

(Pisulewski 2000, Barłowska et al. 2006). This group of fatty acids comprises mostly palmitic acid (C16:0 – 25-30% of total fatty acids) and stearic acid (C18:0) (Pisulewski 2000, Kolanowski 2007). Lauric acid (C12:0) and myristic acid (C14:0) contribute to the risk of cardiovascular disease (Sundram et al. 1994). Stearic acid (C18:0) has a neutral effect. This unsaturated fatty acid is easily converted into oleic acid (C18:1, an unsaturated fatty acid) in the body, and it has been shown to lower blood cholesterol levels. Similarly as lauric acid and myristic acid, also palmitic acid increases the levels of low--density lipoproteins (LDL) and total cholesterol, it contributes to platelet aggregation and the risk of arterial thrombosis. Excessive consumption of palmitic acid increases the risk of cardiovascular disease and atherosclerotic heart disease (Wilke, Clandinin 2005).

The remaining bovine milk fatty acids contain one or more double bonds. Monoene fatty acids have an estimated 30% share of the fatty acid profile, including oleic acid with a 25% share. According to research, the above fatty acids effectively counteract atherosclerosis (Reklewska et al. 2005).

Milk fat contains approximately 3% essential fatty acids (EFAs) which are not synthesized by the body and therefore have to be supplied with food. In the process of dehydrogenation and chain elongation, EFAs are converted into polyunsaturated fatty acids (PUFAs) which contain 2 to 6 double unsaturated bonds. There are two distinct PUFA families, omega-3 (*n*-3) and omega 6 (*n*-6). α-linolenic acid and linoleic acid are heads of the respective families. The proportions of omega-6 to omega-3 fatty acids consumed in the diet should be balanced, and the ideal *n*-6/*n*-3 fatty acid ratio is 4-10:1. Essential fatty acids that deliver the greatest health benefits are C18:2 (linoleic acid) (*n*-3), C18:3 (α-linolenic acid) (*n*-3) and the resulting long-chain fatty acids (containing more than 18 carbon atoms and more than 3 unsaturated bonds), including arachidonic acid (C20:4, *n*-6), eicosapentaenoic acid (C20:5, *n*-3) and docosahexanoic acid (C22:6, *n*-3) (Simopoulos 2002, Dymnicka et al. 2005, Miciński et al. 2012).

The discussed fatty acids are essential components in the diet of infants and children in the first months of life. They play an important role in the development of the central nervous system and the retina. EFAs are bioactive components that lower cholesterol levels and reduce the risk of atherosclerosis. Those prostaglandin precursors are found in cell membrane phospholipids, and they have crucial cellular functions (Reklewska, Bernatowicz 2003).

Oleic acid (*n*-9 family) is one of the most functionally important fatty acids that delivers a variety of health benefits. Oleic acid inhibits the uptake of cholesterol from ingested foods, lowers LDL levels, reduces blood viscosity and lowers blood pressure. Other fatty acids with health-promoting effects include linoleic acid (*n*-6 family) and the resulting arachidonic acid (prostaglandin and leukotriene precursor), as well as fatty acids of the *n*-3 family (eicosapentaenoic acid and docosahexanoic acid). Cell membrane phos-

pholipids contain *n*-6 and *n*-3 polyunsaturated fatty acids. When released from phospholipids, they become a substrate for the synthesis of eicosanoids, including prostaglandins (PG), prostacyclins (PGI), thromboxanes (TXA), leukotrienes (LT) and lipoxins (TURLEY, STRAIN 1993, SIMOPOULOS 2002).

The health effects delivered by polyunsaturated fatty acids can be largely attributed to the activity of eicosanoids, which regulate cardiovascular function, blood pressure, coagulation, plasma triacylglycerol concentrations, immune response, inflammatory processes, proliferation and development of neoplastic cells, hormone and neurotransmitter activity, gene expression, renal function and pain sensation. Eicosanoids prevent ischemic heart disease, they boost immunity, transport lipids, including cholesterol, and lower cholesterol levels in peripheral blood (KOLANOWSKI 2007, KOWALSKI et al. 2010, ZWIERZCHOWSKI et al. 2011).

A deficiency of unsaturated fatty acids can adversely affect growth and development, including weight loss and lower daily gains; it may promote the pathogenesis of many diseases, impair cholesterol transport, increase capillary brittleness and reduce the contractility of the cardiac muscle. Adequate amounts of unsaturated fatty acids in the diet of pregnant women contribute to increasing the birth weight of infants, support the development of the baby's central nervous system, and reduce the risk of allergies and atopic ailments. Unsaturated fatty acids are considered essential for neural and retinal development in newborn babies (BARŁOWSKA, LITWIŃCZUK 2009).

Polyunsaturated fatty acids include conjugated dienes of linoleic acid (CLA) whose double bonds may exhibit cis- and trans-type configuration. CLA is an intermediate product of biohydrogenation of polyunsaturated fatty acids by *Butyrivibrio fibrisolvens* bacteria in the rumen (BARŁOWSKA, LITWIŃCZUK 2009). In a study investigating the CLA content of butter, BAUMAN et al. (2000) isolated bonds with three configuration types: cis-trans, trans-trans and cis-cis. In the above experiment, the CLA content of milk fat was determined at 5.30 g kg^{-1}, and the identified forms had a 85.8%, 9.4% and 4.8% share of total CLA, respectively. According to PARODI (2004), the CLA content of milk fat may exceed 30.00 g kg^{-1}, with a predominance of biologically active isomer cis-9, trans-11. Bovine milk products contain 2.90-11.30 g CLA kg^{-1} of fat, and cis-9, trans-11 CLA has a 73-93% share of this group of fatty acids. Cheese is the richest source of CLA.

CLA has many important functional properties – it impairs the growth of skin, breast, colorectal and gastric cancer cells. The cis-9, trans-11 isomer shows the highest levels of biological activity, whereas the trans-10, cis-12 isomer is believed to prevent the development of obesity (BAWA 2003, WANG, JONES 2004). CLA helps prevent osteoporosis, reduces blood sugar levels, boosts immune system function, lowers total cholesterol and LDL cholesterol levels, and improves the LDL/HDL ratio in the blood plasma, thus contributing to the prevention of ischemic heart disease and atherosclerosis (REKLEWSKA, BERNATOWICZ 2003).

Cholesterol accounts for 0.2-0.4% of total milk lipids. Average cholesterol concentrations are noted at 12 mg in milk with a 3.5% fat content, whereas butter contains 240 mg cholesterol per 100 g fat. In milk lipids, around 90% of cholesterol occurs in free form, whereas the remaining cholesterol is esterified with linoleic acid (18:2), palmitic acid (16:0) and oleic acid (18:1) (ŻEGARSKA 1998). Low density lipoproteins (LDL), high-density lipoproteins (HDL) and very low-density lipoproteins (VLDL) account for 60%, 30% and 10% of total cholesterol in milk lipids, respectively. Saturated fatty acids have varied effects on cholesterol concentrations. Fatty acids which contain 4 to 10 carbon atoms and stearic acid reduce blood cholesterol levels. Lauric acid (C 12:0) and myristic acid (C 14:0) increase the risk of cardiovascular disease, and so does palmitic acid, but only in elderly people (ŻEGARSKA 1998, PARODI 2004).

Milk appears to protect against diabetes. The ingredient responsible is trans-palmitoleic acid, found in milk, cheese, yoghurt and butter, which cannot be synthesized in the human body and has to be supplied by food. On the other hand, eating dairy products may contribute to excessive weight gain and lead to the development of obesity-related diseases, including diabetes, particularly in elderly people (BARŁOWSKA, LITWIŃCZUK 2009).

While milk fat serves as a source of energy for the neonate of each species, it is also a source of bioactive agents which can influence all aspects of physiology from the immune system to the CNS. In addition, its components exert both antibacterial and antiviral activities. In the future transgenesis may provide an approach towards altering the fatty acid composition of milk. The expression of a rat stearoyl-CoA desaturase gene under the control of the bovine β-lactoglobulin promoter in transgenic dairy goats altered the fatty acid composition of milk, resulting in a less saturated and more monounsaturated profile (REH et al. 2004). However, milk fat, unlike other components, is more pliable in that its content can be manipulated through the diet. The ability to manipulate the content of certain fatty acids, such as CLA, has enabled scientists to directly enhance the therapeutic properties of milk and dairy products (MILLS et al. 2011).

Oligosaccharides

Infants and young children digest milk (lactose) easily since they possess specific bacterial flora. The majority of adults, however, lose this ability. Researchers from the University of California in Davis and from the Utah State University (USA) have analyzed the genomes of intestinal bacteria in children and adults. They demonstrated that human milk oligosaccharides (HMOs) are resistant to enzymatic hydrolysis, but they are degraded by some *Bifibobacterium longum* strains. *Bifibobacterium longum* subsp. *infantis* dominates in breastfed infants, and *Bifibobacterium longum* subsp. *longum,* specialized for plant-derived carbon metabolism, is found in adults (MILLS et al. 2011).

The origin of *lactobacilli* and *bifidobacteria* that colonize the neonatal gut had in the past been attributed to contamination of the infant with maternal microorganisms upon passage through the birth canal. However, recent studies provided clear evidence that human milk is a direct source of both *lactobacilli* (MARTIN et al. 2007) and *bifidobacteria* (MARTIN et al. 2009). MARTÍN et al. (2006) successfully tracked a *Lactobacillus salivarius* isolate, which was shown to have potential probiotic properties, from the feces of a one-month-old breast-fed infant to the breast milk of the respective mother through the use of DNA finger-printing. Moreover, in a related study, an analysis of the probiotic potential of another three *Lactobacillus* isolates from breast milk indicated that each strain had probiotic properties comparable to those of strains commonly used in commercial probiotic products (MARTÍN et al. 2005).

A total of 40 oligosaccharides identified in bovine milk are used to produce infant formulas. Most of those oligosaccharides are composed of short oligomeric chains (TAO et al. 2008). Fructo-oligosaccharides and galacto--oligosaccharides (FOS and GOS) are highly effective in promoting the growth of *bifidobacteria* and suppressing the development of pathogenic bacteria in the gastrointestinal tract of newborns and adults (Clostridia and *Escherichia coli*) (BOEHM et al. 2005, FANARO et al. 2005).

FOS are found in vegetables and fruit, such as onions, asparaguses, artichokes and tomatoes (CRITTENDEN, PLAYNE 1996). GOS are produced through the enzymatic conversion of lactose contained in bovine milk (MONTSERRAT, SANTAMARIA-ORLEAN 2001). In 1905, TISSIER (1905) demonstrated that *Bifidobacterium bifidum* is the predominant bacterial species in the intestines of breastfed infants. GYORGY et al. (1974) isolated glycans from milk, which enabled to identify all oligosaccharides (NINONEUVO et al. 2006) – the most important bioactive components of milk (Table 2). Also recent research findings indicate that breastfeeding provides protection against pathogens, and that the use of infant formulas supplemented with the GOS/FOS mixture is an adequate alternative (BAKKAR-ZIERIKZEE et al. 2005, KNOL et al. 2005). The incidence of respiratory inflammation ($p = 0.01$), atopic dermatitis ($p = 0.01$), fever ($p = 0.00001$) and antibiotic use ($p = 0.05$) has been shown to be lower among two-year-olds who were fed formulas supplemented with GOS in the amount of 8 g dm^{-3} for the first six months of their life (MORO et al. 2006, VAN HOFFEN et al. 2009).

It has been estimated that human milk contains 7-12 g dm^{-3} oligosaccharides (BOEHM, STAHL 2007), about 5-10% of the lactose concentration. Milk has a high and relatively stable lactose content (4.5-5.2%), and it also contains trace amounts of glucose and galactose. Lactose is fully synthesized from blood glucose by mammary gland cells. Glucose enhances calcium and phosphorus absorption from food, and it effectively prevents rickets (LITWIŃCZUK et al. 2006).

A comparison of the oligosaccharide content of human milk with milk from other animal species indicates that human milk is unique in terms of the complexity and content of oligosaccharides (KUNZ et al. 2000, BOEHM, STAHL 2007). HMOs reach the maximum concentration in the colostrum (above 20 g dm^{-3}) after which they remain at a stable level in mature milk (approx. 12-14 g dm^{-3}) (COPPA et al. 1999). Bovine milk, on the other hand, contains very low levels of oligosaccharides, around 1 g dm^{-3} (MONTREUIL 1960). In addition to lactose, bovine milk contains trace quantities of glucose and galactose. Glucose promotes the absorption of calcium and phosphorus from milk, thus preventing rickets in children (KOZIKOWSKI, PRZYBYŁOWICZ 1994, LITWIŃCZUK et al. 2004).

Interestingly, milk oligosaccharides have been shown to play a significant role in the induction the inflammatory immune response. Inflammation is a complex multi-step process providing a non-specific defense mechanism against tissue injury. During the inflammatory process, injured tissue cells release chemical signals called inflammatory mediators that activate the endothelium of nearby capillaries. This activation results in the release of cell surface adhesion molecules referred to as selectins, which are glycoprotein in nature, and essential for the formation of plateletneutrophil complexes – PNC (KANNAGI 2002, LEY 2003, RHEE et al. 2003). These heterogeneous cell aggregates represent a large subpopulation of neutrophils with a greater capacity for phagocytosis and increased production of reactive oxygen species – ROS (PETERS et al. 1999).

Calcium and vitamins in milk

Milk lipids are also abundant in vitamins A, D, E and K. One liter of milk covers 25% of the daily recommended intake of β-carotene and vitamin A, and 10% of RDI values for vitamins D and E (PEŁCZYŃSKA 1996, SCHOROEDER et al. 2003). The vitamin A content of bovine milk lipids ranges from approx. 0.60 to approx. 2.00 mg in 100 g of fat, and it is affected by the cow's feeding period (ŻEGARSKA 1998). Vitamins A, E and β-carotene boost the immune system, and they play a significant role in growth, reproduction and vision.

As demonstrated by ZEMEL (2005), calcium found in bovine milk helps us stay slim. It has been suggested that dietary calcium exerts this effect on weight through the calcitrophic hormones, parathyroid hormone and 1,25 (OH) 2 D (ZEMEL 2004). These hormones have been shown to respond to low--calcium diets and exert coordinated regulatory effects on human adipocyte lipogenic and lipolytic systems (ZEMEL 2004). Dairy products may supply 580 mg calcium daily. For optimal results, high calcium intake should be accompanied by an increase in blood vitamin D levels. At high milk consumption, vitamin D concentrations may reach 30 nanograms per milliliter. Researchers from the Ben-Gurion University in Beer-Shera, the USA and

Germany have found that increased calcium intake and high blood levels of vitamin D contribute to weight loss.

Dietary calcium sources, including milk, exert markedly greater effects in attenuating weight than supplemental calcium (ZEMEL 2005). In a study by ZEMEL (2004), 32 obese adults were maintained on balanced calorie-deficit diets – 500 kcal/d and 400–500 mg Ca/d (group I) and 800 mg Ca/d (group II), or a diet high in dairy products (3-4 servings of milk, yogurt, or cheese daily; total calcium intake of 1.20-1.30 g/d). Over the 24-wk trial, group I subjects lost 5.4% of their body mass, compared with 8.6% and 10.9% in groups II and III, respectively (differences significant at $p \leq 0.01$).

The greater effect observed for dairy calcium has been attributed to additional bioactive components which have been assigned to the whey portion of milk (CAUSEY, ZEMEL 2003, ZEMEL 2005). ACE-inhibitory (Angiotensin Converting Enzyme) activity has been postulated as increasing the fat-reducing effects of dairy calcium, since angiotensin-II regulates, in part, adipocyte lipogenesis (PFEUFFER, SCHREZENMEIR 2007). Moreover, branched-chain amino acids (BCAA, leucine, isoleucine and valine) have also been implicated in the process, since in addition to protein synthesis, these amino acids also play specific metabolic roles as energy substrates and in the regulation of muscle protein synthesis (LAYMAN 2003). As already discussed in this review, MCFAs (Medium Chain Fatty Acids) have been shown to have a positive effect on weight reduction. However, not all studies have concluded that dietary calcium or dairy calcium has a positive effect on obesity, and the controversy relating to the results of clinical trials has been discussed in the following reviews (BARBA, RUSSO 2006).

Longer term trials are required to thoroughly investigate the effects of dietary calcium as changes in fat mass may be too small to detect in short periods of time. In addition, several other dietary factors must be considered such as total energy intake, dietary protein content and vitamin D status. Moreover, nutrigenomics has been proving that different populations and different individuals demonstrate variable responses to the same dietary components. BARBA and RUSSO (2006) have suggested that the complex composition of dairy foods may be responsible for this biological variability. Overall, the evidence suggests that dairy foods have an important role to play in weight regulation. In the future, a better understanding of the mechanisms involved in dairy calcium and weight loss will enable reliable recommendations for dairy calcium consumption which will potentially help reduce the development of obesity in many individuals.

Drinking milk after exercise has positive effects in both children and adults. Milk supplies carbohydrates, electrolytes, calcium and vitamin D. Casein and whey contained in milk encourage muscle gain and regeneration. Eating large quantities of dairy products may help achieve longevity. A study involving 4000 human subjects has shown that individuals eating adequate amounts of dairy products (cheese, milk, butter), beginning in early child-

hood, are less likely to have a stroke later in life. Surprisingly, although many dairy products contain fat and cholesterol, their consumption by children does not increase the risk of heart diseases in adults, and it reduces mortality rates by 1/4. Therefore, children should drink a glass of milk every day, eat yoghurt and cheese, and switch to skim milk and milk products at a later age (BARŁOWSKA, LITWIŃCZUK 2009).

Minerals in milk

Milk is a rich source of minerals, mainly calcium, phosphorus, sodium, potassium, chlorine, iodine, magnesium and, in small quantities, iron. Calcium is the key mineral component in milk. Its content largely determines the nutritional value and heat stability of milk, as well as its suitability for cheese production. The average calcium content of bovine milk falls in the range of 0.60-1.20 g dm^{-3} (milk calcium is easily absorbed and is characterized by a high level of physiological activity owing to a favorable calcium to phosphorus ratio of 1.2:1). Milk contains 0.75-1.10 g dm^{-3} of phosphorus, and phosphorus concentrations are generally stable and independent of the nutritional regime of cows. The magnesium content of milk is determined in the range of 100 to 150 mg dm^{-3} In milk, magnesium is found in the form of soluble compounds (75% of total Mg) as well as colloidal compounds (phosphates, citrates). Magnesium concentrations are correlated with the calcium content of milk. Magnesium levels and the magnesium to calcium ratio determine milk's heat stability (NAJERA et al. 2003, KRÓL et al. 2006, LITWIŃCZUK et al. 2006).

Milk has a high content of potassium, sodium and chlorine. It contains 1.35 to 1.55 g dm^{-3} of fully ionized potassium. The sodium content of milk is determined at 350-600 mg dm^{-3}, and chlorine levels are noted in the range of 0.80-1.40 g dm^{-3} (KRÓL et al. 2006). Sodium chloride stabilizes the osmotic pressure of milk (including lactose). A drop in lactose levels resulting from, for example, mastitis, increases the rate of NaCl diffusion from blood. Milk contains trace quantities of iron – 0.42 to 0.45 mg kg^{-1} (GÓRSKA, OPRZĄDEK 2004).

Summary

As a rich source of minerals and nutrients, milk is one of the key components of the human diet. Milk proteins contain readily available amino acids such as lysine, methionine and tryptophan. Milk lipids are abundant in essential fatty acids, and they are characterized by an optimal ratio of omega-3 to omega-6 fatty acids. Bovine milk is also rich in readily available macronutrients and micronutrients (calcium, phosphorus, chlorine, magnesium) which support an array of critical biochemical functions in the human body.

Milk is the natural food which has evolved under selective pressure to meet the nutritional needs of mammalian offspring. Today scientists, members of the Milk Genomics Consortium, are going beyond an analysis of individual milk components to examine the genomics of milk, i.e. the genes that code the composition of milk (GERMAN et al. 2006), with the expectation that such an approach will help describe the principal biological defi-

nition of mammalian nutrition. The future for milk research therefore looks brighter than ever and no doubt will continue in this direction as scientists learn more about milk, yet highly organized food which should serve as a model system for creating superior functional food products (Mills et al. 2011) .

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