Milk Protein

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Introduction

Milk provides the neonate with a readily available complete diet, supplying all essential nutrients. Colostrum, that is, the first milk after parturition, has a considerably higher protein content than later milk. The primary reason for this is the high content of blood-derived immunoglobulins in colostrum compared to milk. Unlike other species such as humans, ruminants lack the ability to transfer immunoglobulins to the fetus *in utero* and are therefore born without immunity. Hence, colostrum, being rich in immunoglobulin proteins, is essential to the early survival of the young calf. In normal milk, the protein content varies considerably between species, from a low of $1\,g\,l^{-1}$ in humans to a high of $145\,g\,l^{-1}$ in the black bear, and cow's milk contains approximately $32–35\,g\,l^{-1}$ (*see* **Mammary Gland, Milk Biosynthesis and Secretion**: Lactose, Table 1).

Through improved nutrition, breeding, and management, milk production of the modern dairy cow is well in excess of that required to feed its offspring. Milk is an important product to man, in terms of both nutritional and economic values. At present, protein, and in particular casein, is the most valued milk component, being the principal ingredient of cheese. Until recently, whey proteins were considered to be of limited value and were often disposed of as waste or used as an animal feed. However, various specific whey proteins are now being valued for their bioactive properties.

Milk Protein Composition

Milk protein is made up of a large number of different small and large proteins. Most milk proteins are mammary-derived, synthesized within the secretory epithelium of the mammary gland and secreted into the milk pool within the alveolar lumen. The mammary-derived milk proteins can be further divided into two broad categories: casein and whey proteins. The classical method to distinguish between the two is by acid precipitation of defatted milk. Caseins precipitate when milk is acidified to a pH of approximately 4.6, but the whey proteins remain in solution. Ruminant milk contains four different caseins: α-casein, β-casein, κ-casein, and γ-casein (Table 1). The first three caseins are expressed by different genes, and different cows may carry different genetic variants of each of the caseins. γ-Caseins are the breakdown products cleaved from β-casein by the major milk proteolytic enzyme plasmin (EC 3.4.21.7). In milk, casein molecules appear as micelles, which are spherical structures consisting of many thousands of individual casein molecules linked together and encapsulating significant amounts of calcium and phosphate and to a lesser extent citrate. The major whey proteins synthesized by the ruminant mammary gland are α-lactalbumin and β-lactoglobulin (Table 1). Interestingly, α-lactalbumin plays a crucial role in milk lactose synthesis as part of the enzyme lactose synthetase (EC 2.4.1.22; *see* **Mammary Gland, Milk Biosynthesis and Secretion**: Lactose). In addition to milk proteins, the mammary gland also synthesizes a number of constitutive proteins, such as structural proteins, enzymes, hormones, and growth factors. These proteins play an important role in mammary function, and they may be secreted into milk, but are mostly turned over within the mammary gland.

Finally, in addition to proteins that are synthesized within the mammary gland, the whey fraction of milk contains a large number of smaller proteins that are taken up from the blood and transported without further processing across the secretory cell into the milk, via either a transcellular route or a paracellular (i.e., between adjacent mammary epithelial cells) route. Examples of such blood-derived and mostly immune-related proteins are immunoglobulins, lactoferrin, lactoperoxidase, and serum albumin. Some are taken up into the mammary cell by active transport mechanisms, whereas others enter by passive diffusion or by a process of internalization, and for some it is not yet known exactly how they enter the secretory cells of the mammary gland.

Biosynthesis and Secretion

The milk protein substrates (amino acids) are supplied to the mammary gland by the blood. Arteriovenous difference studies have demonstrated the remarkable capacity of the mammary gland for extracting amino acids from the blood. The actual movement of amino acids through the basolateral membrane of the secretory cell is facilitated by several sodium-dependent or sodium-independent amino-acid transport systems, with different transporters being specific to the transport of different groups of amino acids.

Table 1 The content and composition of protein in creamery milk in south-west Scotland

		Skim milk ($g\,l^{-1}$)		*Total protein (%)*		*Total casein (%)*		*Total milk serum protein (%)*	
	Mammary or blood derived	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Total protein	-	32.71	1.80	-	-	-	-	-	-
Total casein	-	26.92	1.54	82.2	0.6	-	-	-	-
Total milk serum protein	-	5.79	0.32	17.8	0.6	-	-	-	-
α_{s1}-Casein	Milk	10.25	0.57	31.3	0.5	38.1	0.5	-	-
β-Casein	Milk	9.60	0.50	29.3	0.6	35.7	0.8	-	-
κ-Casein	Milk	3.45	0.32	10.5	0.5	12.8	0.6	-	-
α_{s2}-Casein	Milk	2.74	0.21	8.4	0.5	10.2	0.8	-	-
γ-Casein	Milk	0.88	0.15	2.7	0.4	3.2	0.4	-	-
β-Lactoglobulin	Milk	3.14	0.19	9.6	0.4	-	-	54.2	1.3
α-Lactalbumin	Milk	1.23	0.09	3.8	0.3	-	-	54.2	1.3
IPL	Blood	0.97	0.10	3.0	0.2	-	-	21.2	1.4
Bovine serum albumin	Blood	0.45	0.04	1.4	0.1	-	-	7.8	0.6

Values are the mean of 29 samples from five creameries.
IPL, immunoglobulins, proteose-peptone component 3, and lactoferrin; SD, standard deviation.
Adapted from Davies DT and Law AJR (1980) The content and composition of protein in creamery milks in south-west Scotland. *Journal of Dairy Research* 47: 83–90.

Once inside the secretory epithelium, the basic process of using the amino acids for protein synthesis in the mammary gland does not differ from that occurring in other tissues within the body (**Figure 1**). Milk proteins, as any other proteins, are encoded by different genes that help make up the genome. The biosynthesis of proteins is initiated by factors (e.g., hormones) that induce gene expression. The actual initiation of gene expression is a complex process involving interactions between hormone-induced nuclear transcription factors and the promoter area or specific enhancer regions of the DNA upstream of the promoter. Gene expression occurs in all tissues and is not unique to the mammary gland. A detailed description of these processes is therefore beyond the scope of this article.

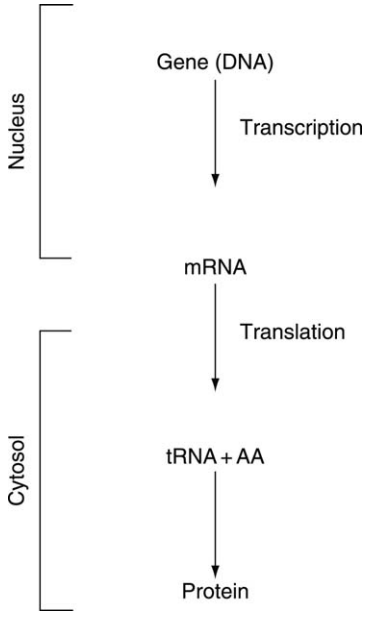

Figure 1 General pathway for protein synthesis. Transcription occurs in the nucleus of the cell, whereas translation occurs on the ribosomes on the rough endoplasmic reticulum. AA, amino acids; mRNA, messenger RNA; tRNA, transfer RNA.

Expression of the gene encoding a protein starts with making a mirror image of the gene's DNA template with the help of the enzyme RNA polymerase (EC 2.7.7.6). The resulting image or messenger RNA (mRNA) is complementary to the DNA template, but differs slightly in that RNA contains the base uracil instead of thymidine. The resulting mRNA now forms the blueprint for the protein and determines the sequence of the amino acids that make up the particular protein. Thus far, the process has occurred in the nucleus of the cell; however, the mRNA then moves from the nucleus into the cytosol and to the ribosomes on the rough endoplasmic reticulum (RER). On the ribosomes, the mRNA is translated into protein. Each successive nucleotide triplet in the mRNA codes for a specific amino acid and as the mRNA moves through the ribosome the appropriate amino acids are linked together with the aid of transfer RNA (tRNA).

Interestingly, evidence is emerging that in addition to the classical regulation of gene expression, as described before, milk protein expression may also be under epigenetic regulation. It was recently shown that DNA methylation at specific sites on the αs1-casein promoter was able to downregulate the expression of αs1-casein during certain physiological conditions.

Milk proteins are secretory proteins and have to be exported from the cell into the milk pool in the alveolar lumen. To facilitate the movement of a secretory protein into the RER, an amino-terminal signal sequence of approximately 20 hydrophobic amino acids is added to the protein to guide it through a membrane channel in the wall of the RER. Even before translation of the protein is completed, the signal peptide is cleaved from the protein by a proteolytic enzyme (signal peptidase; EC 3.4.21.89) and is inserted into the membrane channel. After completion of the translation process and following translocation into the inside of the RER, the (milk) protein has now been formed; however, this does not necessarily mean that it is also a functional protein. In order for the protein to become functional, it must be folded into its appropriate three-dimensional structure. Moreover, other molecules such as carbohydrates (in the case of glycoproteins), phosphate groups, and ions may be attached to the protein. In the case of caseins, many casein molecules (as many as 25 000) group together to form large micelles. These processes occur en route to and in the Golgi apparatus, from where the proteins, together with lactose, are encapsulated in secretory vesicles that bud off the Golgi and are moved with the aid of the cytoskeleton toward the apical membrane. There, the secretory vesicles fuse with the apical membrane and release their contents including proteins, lactose, ions, and water into the milk pool of the alveolar lumen.

Factors Affecting Milk Protein Synthesis

Diet

Like any other tissue where protein synthesis occurs, the mammary gland has a requirement for nonessential and essential amino acids. The only difference with other tissues is that the mammary gland is a secretory organ that can produce and export into the milk vast amounts of milk protein, and as such has a very substantial demand for substrates. The required substrates are supplied via the mammary arterial blood supply and the diet determines to a large extent the amount and type of substrate available for mammary uptake. However, it is pertinent to point out that there is a distinct difference in dietary protein digestion between ruminants and nonruminants. In the latter, the breakdown of proteins starts in the stomach with the production of hydrochloric acid and the enzyme pepsin (EC 3.4.23.1), and is completed in the small intestine where a series of other proteolytic enzymes such as trypsin (EC 3.4.21.4) and amino- and carboxypeptidases further break down the dietary protein. The ultimate breakdown products, amino acids and small peptide fractions, are absorbed across the intestinal wall and used for protein synthesis and/or gluconeogenesis. The composition of the diet determines directly which proteins are presented for digestion. Although the same processes occur in ruminants, all food has to pass first through the rumen before it moves on to the stomach and intestines. Approximately two-thirds of all dietary protein is broken down in the rumen by bacteria and protozoa and converted into microbial protein. It is this microbial protein that is presented to the lower digestive tract, together with the roughly one-third of dietary protein that escapes degradation in the rumen, the so called bypass protein. Although it may not appear to be all that efficient to have this extra compartment (i.e., the rumen) where dietary protein is converted first to microbial protein before it enters the stomach, one must remember that this unique system allows ruminants to digest large amounts of plant material, sometimes of low quality, and convert it into high-quality microbial protein. This also means that in ruminants the protein composition of the diet has relatively less effect on milk protein composition and that the essential amino-acid composition of the diet is less critical, because of the ability of the rumen microbes to synthesize essential amino acids.

This does not mean that diet cannot influence milk protein production. To the contrary, simply increasing the crude protein content of the diet may increase milk protein yield, but different experiments do not always give consistent results, due to differences in the level and composition of the basal diets. Experiments to determine the effect of extra dietary protein on milk protein production often involve the infusion of casein protein postruminally. Using casein, one is assured that the extra amino acids supplied by the diet are the right ones for milk protein synthesis, and infusing them postruminally prevents the conversion of the dietary casein protein into microbial protein. A positive effect on milk protein synthesis of such additional dietary protein depends very much on the composition of the basal diet, and is observed only when the basal diet is energy deficient or is low in protein. Similarly, the best response is seen in very high-yielding cows, which are more likely to be in a negative energy balance. Increasing the degradable carbohydrate fraction of the diet may also have a positive impact on milk protein synthesis, either through supplying more energy to the rumen microbes and thus enhancing microbial protein production and substrate supply to the mammary gland, or by increasing the supply of energy substrates to the mammary gland, allowing for increased amino-acid utilization.

In summary, the success, in terms of increasing milk protein output, of any dietary manipulation depends on delivering the right substrates to the mammary gland. For example, methionine is generally considered a limiting amino acid in ruminants, and including protected methionine to bypass rumen degradation increases milk protein content, in particular in cows on low-protein corn-based rations. Lysine is often considered to be another limiting amino acid in ruminants, but the effects of additional

lysine on mammary protein synthesis are less straightforward since the net mammary uptake often exceeds the output into milk, but this may be due to substantial intramammary oxidation of lysine.

Endocrine Control

Endocrine factors play an important role in the induction and regulation of gene expression in all tissues, and the mammary gland is no exception. The results from *in vitro* experiments with either mammary cell or explant cultures, and also those from *in vivo* experiments with predominantly rodents, indicate that prolactin, insulin, and cortisol (hydrocortisone) are the essential hormones required for milk protein synthesis. In contrast, progesterone has been shown to decrease casein and α-lactalbumin accumulation in mammary explants of mice. This, however, may be related to progesterone's role as a general inhibitor of lactation, rather than a direct effect on protein secretion *per se*. Similarly, continuous infusion of glucagon into early lactation dairy cows showed a transient negative effect on milk yield and milk protein content. Again this is unlikely to be a direct effect of glucagon on milk protein gene expression, but rather relates to the effect of glucagon on amino-acid availability to the mammary gland. A concurrent transient decrease in feed intake and an increase in gluconeogenesis from amino acids by the liver are likely responsible for the decrease in substrate supply.

Studies at Cornell University, examining the role of insulin in mammary protein synthesis in cows, demonstrated quite clearly that even in high-yielding dairy cows protein synthesis has not yet reached its maximum capacity. These studies, which used the hyperinsulinemic-euglycemic clamp technique, showed that insulin was able to increase mammary protein output in addition to an increase resulting from abdominally infused casein protein (**Figure 2**). Thus, even after optimizing dietary conditions, further gains may be achieved through endocrine manipulation.

How exactly endocrine factors can enhance milk protein synthesis is not clear. Increasing substrate supply by increasing mammary blood flow, both at the arterial and microvascular level is, however, a distinct possibility, as is increasing mammary uptake of substrates via effects on membrane transporter systems. However, another important area may be the reduction of intramammary protein turnover. The turnover of constitutive proteins (e.g., enzymes) and casein in the mammary gland may be as high as 40–70%. This means that a significant proportion of synthesized milk proteins are not secreted, which clearly contributes to the rather low overall efficiency of 20–30% with which dietary nitrogen is converted into milk protein.

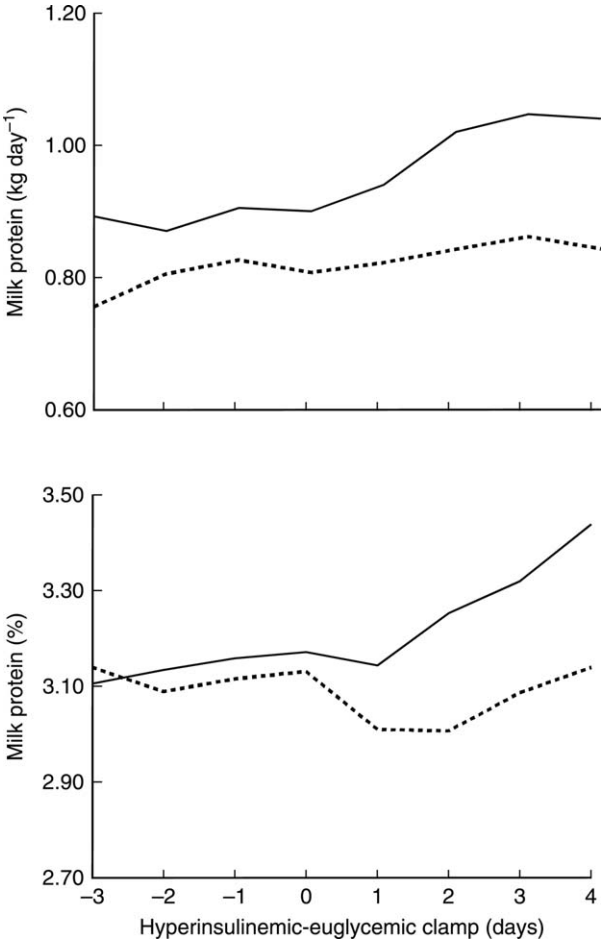

Figure 2 Protein yield and concentration in milk from cows ($n = 5$) during the baseline interval (−3 to 0 days) and 4-day (0–4 days) exposure to an insulin infusion (1 μg per kg body weight per hour) using a hyperinsulinemic-euglycemic clamp. In addition, throughout the experiment, cows received abomasal infusions of water (dashed lines) or casein (solid lines). Casein infusion improves mammary protein synthesis, but infusion of insulin improves protein synthesis even further. (Insulin clamp technique: insulin acts to maintain constant blood sugar levels, and infusion of insulin would result in a dangerous drop in the blood glucose level; therefore, during the clamp technique, glucose is infused concurrently to maintain the blood glucose level, while insulin levels are elevated.) From Griinari JM, McGuire MA, Dwyer DA, Bauman DE, Barbano DE, and House WA (1997) The role of insulin in the regulation of milk protein synthesis in dairy cows. *Journal of Dairy Science* 80: 2361–2371.

Temperature

Ambient temperatures on either side of the thermoneutral zone affect milk protein synthesis. Numerous studies report that heat stress has an adverse effect on mammary protein synthesis, whereas providing shade during hot weather conditions may prevent the drop in protein production. It is not clear if this is the result of a direct effect on mammary protein synthesis, or instead due to an indirect effect of altered mammary substrate supply.

During hot weather, food intake is reduced and the metabolic rate is lowered to prevent the body from overheating. Endocrine changes also occur, most notably systemic reductions in thyroxine and cortisol, and an increase in prolactin. Given the importance of prolactin for mammary protein synthesis, these contradictory effects would argue against a direct effect of heat stress on milk protein synthesis. In contrast to studies examining the effects of heat stress on milk production, there are considerably fewer studies examining the effects of cold stress. However, the limited available data suggest an increase in milk protein when animals are exposed to below 0 °C temperatures. Systemic prolactin concentrations are reduced during cold exposure, arguing again against a direct effect on milk protein synthesis. Feed intake increases during cold stress and the levels of the stress hormone epinephrine also increase, causing an increased rate of lipolysis. All these increase the energy supply to support an increased metabolic rate and probably increase mammary substrate availability.

Milking Frequency

Tight junctions are the cellular structures that prevent the intercellular movement of blood and/or milk components between adjacent secretory cells of the mammary epithelium. As discussed in more detail in **Mammary Gland, Milk Biosynthesis and Secretion**: Lactose, more or less frequent milking than twice a day will result, respectively, in tighter or 'leaky' tight junctions. Leaky tight junctions will affect the whey protein composition of the milk, as small mammary-derived milk proteins, such as α-lactalbumin, will 'leak' from the milk via this paracellular route into the blood, whereas small blood proteins, such as proteolytic enzymes (e.g., plasmin), serum albumin, lactoferrin, and immunoglobulins, may leak into the milk pool. More frequent milking tends to tighten the tight junctions and prevents these changes from occurring.

Stage of Lactation

The protein content of milk changes considerably during lactation. The first milk after calving (i.e., colostrum) is very high in protein (approximately $230\,g\,l^{-1}$). This is mainly due to the large amount of immunoglobulins in colostrum. Within days of parturition, colostrum changes into regular milk, which is of much lower protein content. The milk protein content is lowest around 8 weeks into lactation, which coincides with the maximum negative energy balance of the cow, that is, with the maximum gap between energy intake from the feed and output via the milk is the largest. Hence, the low rate of mammary protein synthesis at this time is most likely related to insufficient substrate supplies to the mammary gland. As lactation progresses and the animal switches to a positive energy balance, milk protein content gradually increases. Toward the end of lactation, the whey content of milk starts to increase. This is the result of a gradual loosening of the tight junctions between the epithelial cells and is indicative of the onset of gradual mammary gland involution.

Mastitis

Mastitis is an inflammation of the mammary gland and is, in most cases, the result of a pathogenic infection. As such, there is a rapid influx of immune cells into the gland and subsequently into the milk. Most notably, the level of neutrophils increases rapidly with the onset of mastitis. The increase in cells in milk manifests itself in an elevated level of somatic cells. Indeed, the most commonly used on-farm indicator of mastitis is an elevated milk somatic cell count. In addition to immune cells, mastitic milk contains a vast array of peptides and proteins representing both the adaptive immune system (e.g., immunoglobulins, complement) and the innate immune system (e.g., cytokines, lactoferrin, lactoperoxidase, RNases, acute-phase proteins). Not only do these host defense peptides and proteins markedly change the whey protein composition of milk, the casein proteins may also be affected by mastitis. The casein content of milk will be reduced as mastitis causes an increase in plasmin activity in milk, which, as pointed out at the beginning of this article, degrades β-casein, resulting in an increase in γ-caseins.

Breed Differences

The previous factors have all been environmental, that is nongenetic factors, but it is well known that on average, milk composition, and in particular milk protein content, varies among the major dairy breeds. The protein content of milk from Jersey cows is significantly higher than the protein content of milk from Holstein-Friesian cows. However, the latter produce more milk, such that total milk protein production is higher in Holstein-Friesian cattle.

As mentioned earlier, different genetic variants exist for each of the major whey and casein proteins. In most dairying countries, there is considerable interest in exploiting such within- and among-breed polymorphisms, as increased contents of certain variants may have beneficial influences on the processing properties or may result in increased cheese yields. For example, milk from β-lactoglobulin AA cows contains more whey protein, whereas that from BB cows has more casein, and also better processing properties, such as higher curd tensions. Indeed, BB milk has been shown to give higher yields of certain cheeses (e.g., Parmesan and Gouda cheese).

Table 2 Examples of substances with biological activity present in milk[a]

Bioactive function	*Bioactive component*	*Chemical nature*	*Remarks*
Antibacterial	Lactoferrin, lactoperoxidase, lysozyme, defensin	Peptide	Can be added to infant formula, tooth paste, and cosmetics. May also be used to increase the shelf life of products
Gastrointestinal function (intestinal motility, emptying, absorption)	Casomorphin, lactorphin	Peptide	Casein-derived fragments with opioid agonistic activity
	Casoxin	Peptide	Casein-derived fragments with opioid antagonistic activity
	Serophin	Peptide	Opioid activity; derived from serum albumin
	Lactoferroxin	Peptide	Opioid antagonistic activity; lactoferrin-derived
	β-Lactotensin	Peptide	Affects the smooth muscle of the gut; β-lactoglobulin-derived
	Albutensin	Peptide	Affects the smooth muscle of the gut; serum albumin-derived
	Caseinomacropeptide	Peptide	Increases gut motility and CCK and gastrin release; κ-casein-derived
Cell growth and repair	Growth factors (e.g., IGF-I, EGF, TGF-α), growth inhibitory factors (MDGI, TGF-β)	Peptide	Play a role in the regulation of cell growth and repair in many different tissues (e.g., intestines); also used as supplements in cell culture media
	β-Casein-derived fragments	Peptide	Cell growth promoting
	Glutamylcysteine	Peptide	Stimulates glutathione, an antioxidant involved in cell protection and repair
	Lactoferrin	Peptide	Involved in cell protection and repair (antioxidant)
Hypertension lowering	ACE inhibitors	Peptide	Inhibits ACE, preventing the conversion of angiotensin-I into the active vasoconstrictor angiotensin-II
	Calcium	Mineral	
Mineral utilization	α_{s1}-, α_{s2}-, and β-casein-derived phosphopeptides	Peptide	Sequester minerals in soluble complexes for easy intestinal absorption (e.g., calcium, iron, manganese, selenium)
Bone synthesis	Calcium	Mineral	Promotes bone growth
	Hormone (PTHrP)	Peptide	Calcium uptake
Immunoregulation	Lactoferrin		
	Immunoglobulins	Peptide	Provide passive immunity. Bovine milk is a rich source of IgG and to a lesser extent IgA
	α- and β-casein-derived fragments	Peptide	Immune-enhancing properties
	Cytokines	Peptide	Stimulate lymphocyte trafficking and development of immune system
	Minerals (zinc, iron, copper, selenium) and vitamins (A, β-carotene, B_6, C, E)		Cofactors in many immune processes, and as such immunostimulatory
Anticarcinogenic	CLA	Lipid	Anticarcinogenic properties (in particular against mammary cancer)
	Sphingolipids (sphingomyelin, ceramides, gangliosides)	Glycolipids	Phospholipids of cell membranes. Inhibit cell growth and may suppress tumor growth
Increasing lean body mass	CLA	Lipid	Reduces body fat and enhances lean body mass
Prebiotics/probiotics	Galacto-oligosaccharides	Carbohydrate	Enhance the growth of beneficial bifidobacteria in the gut. Lactose derived; the disaccharide lactose is extended with β-galactosidase to form oligosaccharides
Atherosclerosis	CLA	Lipid	There is some evidence from animal studies that CLAs may lower cholesterol

[a]Information collected from various refereed and nonrefereed publications.

ACE, angiotensin converting enzyme; CCK,cholecystokinin; CLA, conjugated linoleic acid; EGF, epidermal growth factor; IGF, insulin-like growth factor; MDGI, mammary-derived growth inhibitor (homologous to fatty acid binding protein); PTHrP, parathyroid-related peptide; TGF, transforming growth factor.

Bioactive Milk Proteins

Bioactives are substances that consist of protein, lipid, and/or carbohydrate molecules and are capable of eliciting a biological response, such as reducing hypertension, preventing cancer, enhancing lean body mass, stimulating the immune system, and killing bacteria. Increasingly, milk is considered to be a rich source of such bioactives (**Table 2**). The first published results of proteomic analysis of milk, using powerful proteomic tools, revealed more than 90 different minor milk peptides and proteins, and many are thought to play a role in mammary host defense. Many of them are proteins or peptides that exist in very low concentrations in the whey fraction of milk. Some of them are blood-derived, whereas others may be synthesized within the mammary gland either directly or indirectly via breakdown of casein molecules (e.g., casomorphins).

Traditionally, caseins have been considered the most valuable proteins in milk given their importance for cheese manufacturing. Whey proteins, on the other hand, have long been considered to be of little value and were often disposed of as waste or returned to the farmer to be used as calf or pig feed; however, this has changed now and there is a market for whey products such as whey protein concentrates and lactoferrin. Bovine milk-derived lactoferrin is now a common ingredient in human and pet foods, cosmetics, or oral and skin care products. Moreover, bovine colostrum is now widely available as an immune-stimulating health supplement for human consumption. The importance of milk whey peptides and proteins is likely to increase further with the development of more advanced technology to detect and extract bioactives from milk. Although the yields of bioactive proteins are very low compared to the major milk proteins, they are included in products at the high end of the market (e.g., cosmetics, infant formula, biomedical products, and sport enhancing and health food products) yielding high financial returns. Such value-added products will certainly have positive impact on future milk prices. Whether casein will ever become a by-product of whey, as has been suggested, remains to be seen, but there is no doubt that milk-derived bioactive products will play an important role in the future success of the dairy industry.

Health Disorders

Humans may suffer from milk protein allergies after consuming dairy products. Allergies against milk proteins can occur in patients of all ages, but are most common in infants. Double blind studies have shown that up to 2% of infants may suffer from such allergies. Bovine milk proteins and their fragments are foreign to the human body, in particular β-lactoglobulin, which does not occur in human milk, and are recognized by the immune system as any other antigen, and as such can elicit an immune response. The prerequisite is, however, that the milk proteins or fractions thereof cross the intestinal wall into the bloodstream without being digested into amino acids. This occurs only in patients who suffer from a 'leaky gut' or compromised intestinal wall as a result of gastroenteritis, Crohn's disease, or gastrointestinal bleeding. In infants, it is probably related to insufficient or a delay in the natural process of closure of the intestinal wall after birth. Processing steps, such as hydrolysis, may help to lessen the allergenicity of milk proteins. Some claim that infants that are allergic to cow's milk are better off drinking goat milk-based products; however, the proteins in goat's milk are just as foreign to the body as those in cow's milk, and the same holds true for soy protein-based infant formula. That goat milk appears to be overall less allergenic than cow's milk may be related to the fact that the former contains a lower level of αS1-casein. Moreover, goat β-lactoglobulin appears to be broken down more effectively by humans than its bovine counterpart. Ironically, it has become increasingly evident from experiments that milk and colostrum components (bioactives) have beneficial effects on intestinal development and on the prevention of compromised gut syndrome (**Table 2**). There is even some evidence emerging from international epidemiological studies suggesting that raw, unpasteurized, bovine milk may have antiallergenic properties.

See also: **Mammary Gland, Milk Biosynthesis and Secretion**: Lactose.

Further Reading

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