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Milk Proteins' Polymorphism in Various Species of Animals Associated with Milk Production Utility

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1. Introduction

In the recent years a significant progress has occurred in the understanding of many of the complex processes in cells of the body at a molecular level. To clarify the basis of this phenomenon the development in the field of molecular biology was a great contribution. This area has provided many hitherto unknown tools that enabled the understanding of fundamental life processes at a basic level. The utilization of the achievements of biological and zootechnical sciences led to a significant increase in animal productivity.

The first research studies concerning the detection of genetic diversity among farm animals were based on morphological, chromosomal and biochemical markers and therefore, they are not free of defects. Most of the morphological markers are limited by gender or age and are influenced by the environment. The biochemical markers, however, contribute to low levels of polymorphism (Boichard et al., 2003; Naqvi, 2007). Currently a key role in animal genetics is connected with molecular markers. Molecular markers are specific pieces of DNA that can be identified within the genome and are inherited according to Mendel's laws (Teneva & Petrović, 2010). They can be successfully utilized to detect and track the inheritance mechanisms of polymorphic traits that contribute to genetic diversity (Khatkar et al., 2004). Molecular markers which enable the detection of genetic variants at DNA sequence level are devoid of these limitations typical for morphological, chromosomal and protein markers. They also have unique properties that make them more useful than other markers. They are ubiquitous throughout the genome, often multi-allelic, giving an average heterozygosity of more than 70%. What is more, molecular markers are not influenced by environment and usually do not have pleiotropic effect on quantitative traits loci (QTL) (Teneva, 2009).

Up to date, numerous techniques of studying DNA variations at the molecular level are known. The most famous include RFLP (restriction fragment length polymorphism), SNP (single nucleotide polymorphism) and STR (microsatellite DNA polymorphism) (Beuzen et al., 2000; Teneva & Petrović, 2010).

RFLP (restriction fragment length polymorphism)

Restriction fragment length polymorphism (RFLP) is associated with the occurrence of differences in nucleotide sequences in the gene. It is a result of point mutations, which may manifest themselves phenotypically. They appear through the use of restriction enzymes that recognize sequences specific to their nucleotide. The mutations result in the creation of new places that are identified by restriction enzymes that cut DNA into fragments of various lengths. This technique consists of amplification of specific parts of the genome and the amplicon is digested by one or more restriction enzymes. The obtained DNA fragments are distributed on an agarose gel and, depending on their size, migrate at different speed rates. Smaller fragments tend to move faster in the comparison to larger ones (Beuzen et al., 2000; Bogdzińska, 2011; Marle-Köster & Nel, 2003).

SNP (single nucleotide polymorphism)

The system enables detection of single nucleotide polymorphism within the examined DNA sequences. It is based on the amplification of specific parts of the genome in the PCR reaction and sequencing of the product obtained. A comparison between electrophoresis images of amplification products is conducted, which allows determining whether a mutation in a given region had occurred. Point mutation leads to the formation of a polymorphic SNP if each of the alleles appear in the population with the frequency not lesser than 1 %. What is more, these markers are present in both coding and non-coding parts of the genome (Stoneking, 2001). SNP polymorphism is usually associated with the presence of only two alleles in the gene pool of the population (Beuzen et al., 2000). On the one hand, a great advantage of this polymorphism is its universality in the genome of different species and highly efficient identification of polymorphism within the tested sequence while on the other hand, the high cost of the analysis makes it a disadvantage. The high density of SNP markers in the genome leads to their extensive utilization in the genetic analysis (Charon & Świtoński, 2000).

Microsatellite DNA

Genetic diversity may be also determined by utilization of microsatellite sequences. This group of markers is polymorphic in more than 90 % of the cases. Microsatellites are also known as simple sequence repeats (SSR) or short tandem repeats (STR). These repeats consist of several nucleotides (1-6) sequences also referred to as motifs. They are repeated from 20 to 50 times and their lengths range from 60 to 300 bp (Ellegren, 2004; Liu & Cordes, 2004). They occur mainly in non-coding regions of the genes, thus they can be also identified in flanking sequences or more rarely in coding sequences. What is more, they are characterized by uniform dispersion at 6 000 to 10 000 bp (Li et al., 2004; Liu et al., 2001). The function of microsatellites is not yet fully understood (Li et al., 2002). Probably through the

dispersion across the genome they have an impact on increasing or decreasing the expression of genes (Pisarchik & Kartel, 2000). Features of microsatellites like high level of polymorphism, high frequency of occurrence, ease of identification and uniform distribution across the genome contributed to their common usage. They are used in the estimation of the genetic variability of animals, in the research on the control of origin, to characterize the structure and degree of inbreeding of the population and also to identify the genes of quantitative traits (QTL). What is more, they are used to conduct the selection based on genetic markers (MAS- *Marker Assisted Selection*) (Citek et al., 2006).

In the evaluation procedure of animals breeding value the knowledge of genome organization and polymorphism is increasingly utilized due to the fact of vast and easy access to many molecular technics. What is more, many mutations directly affecting the phenotype were recognized. On the other hand, thousands of anonymous genetic markers, because of their potential linkage with novel mutations of large scale of activity, may be utilized for estimation of the breeding values and selection based on genetic markers (MAS).

2. Location of genes and the frequency of alleles conditioning the synthesis of selected milk proteins in most species of animals used for milk productivity

The major milk proteins include casein: α_{S1} -, α_{S2} -, β -, κ - and two whey proteins: α -lactalbumin and β -lactoglobulin. These fractions, in most species, are polymorphic.

2.1. Cattle

Polymorphism of milk proteins has been widely explored in the case of cattle. Cattle casein *loci* is located on chromosome 6 (6/BTA 6q31-33) and occupies a total DNA fragment of 200 kb. Genes are arranged in order: CSN1S1, CSN2, CSN1S2, CSN3 and encode, respectively: α_{S1} -casein, α_{S2} -casein, β -casein and κ -casein. These genes are closely linked and form a cluster (Bai et al., 2008; Caroli et al., 2009).

α_{S1} -casein is a fraction which forms up to 40 % of bovine caseins in milk. It consists of one major and one minor component. Both of these proteins are composed of a single polypeptide chain of the same amino acid sequence. The reference protein for this family is α_{S1} -CN B-8P, a single chain protein with no cysteine residues. It consists of 199 amino acids residues: Asp₇, Asn₈, Thr₅, Ser₈, Ser P₈, Glu₂₅, Gln₁₄, Pro₁₇, Gly₉, Ala₉, Val₁₁, Met₅, Ile₁₁, Leu₁₇, Tyr₁₀, Phe₈, Lys₁₄, His₅, Trp₂, and Arg₆ with a molecular mass of 23.615 (Mercier et al., 1971). So far 8 alleles were identified within the α_{S1} -casein: A, B, C, D, E, F, G and H (Farrell et al., 2004). The most frequent, however, are alleles B and C found both in dairy and beef cattle (Litwińczuk et al., 2006). For European cattle breeds allele B is the most common – it exceeds the frequency of 0.9 (Kučerova et al., 2006; Luhken et al., 2009). Allele B at the 192 position of the polypeptide chain encodes glutathione, whereas the allele C encodes glycine. Variant A occurs sporadically. Alleles C, D and E were created due to the mutation of allele B. Table 1 shows the frequencies of α_{S1} -casein alleles in various breeds of cattle.

Cattle breed	Allelic frequencies of α_{S1} -casein	References
Holstein-Friesian	B = 0.981 C = 0.019	Çardak, 2005
Simmentaler	B = 0.932 C = 0.068	
Reggiana	B = 0.750 C = 0.250	Caroli et al., 2004
Uruguayan Creole	B = 0.8654 C = 0.1346	Rincón et al., 2006
Polish Red	B = 0.928 C = 0.042 D = 0.030	Erhardt et al., 1998
Red Danish Dairy Cattle	A = 0.003 B = 0.994 C = 0.003	
German Red	B = 0.975 C = 0.025	
Czech Fleckvieh	B = 0.893 C = 0.107	Kučerova et al., 2006
Hereford and crossbreeding F ₁ and R ₁ (Black and White x Hereford)	A = 0.025 B = 0.710 C = 0.136 D = 0.130	Litwińczuk & Król, 2002
Limousine and crossbreeding F ₁ and R ₁ (Black and White x Limousine)	A = 0.020 B = 0.617 C = 0.214 D = 0.148	
Simmentaler	B = 0.750 C = 0.250	
Estonian Native	B = 0.915 C = 0.085	Jõuru et al., 2007
Western Finncattle	B = 0.939 C = 0.061	
Danish Jersey	B = 0.781 C = 0.219	
Brazilian Zebu cattle (Gyr, Guzarat, Sindi, Nelore)	B = 0.000 – 0.136 C = 0.864 – 1.000	Da Salva & Del Lama, 1997

Table 1. The frequencies of α_{S1} -casein alleles in various breeds of cattle

The gene CSN1S2 encoding α_{S2} -casein has the length of 18 438 nucleotides and is divided into 18 exons ranging from 21 to 266 nucleotides (Ramunno et al., 2001). So far only 4 genetic variants of bovine α_{S2} -casein were described: A, B, C and D. Allele A which was created by

mutation of allele D exists in most European breeds up to date. Alleles B and C are specific, respectively, for zebu and yaks (Ibeagha-Awemu et al., 2007).

β -casein is a fraction which forms up to 45 % of bovine caseins in milk. The native milk protease plasmin leads to the creation of γ_1 -, γ_2 - and γ_3 -CN, which are actually fragments of β -casein consisting of the following sections of the chain 29-209, 106-209 and 108-209 (Farrell et al., 2004). 12 genetic variants that determine the synthesis of this protein were identified so far, i.e. A¹, A², A³, B, C, D, E, F, G, H¹, H² and I (Farrell et al., 2004). The reference protein for this family is β -casein A2-5P consisting of a single chain protein, assembled from 209 amino acids residues without cysteine residues. The most common forms of β -casein in dairy cattle are A¹ and A², which differ by only one amino acid (Farrell et al., 2004). At the 67 position of amino acid chain, respectively, variant A¹ contains histidine and variant A² proline. Variant A², however, is the original form and is identified in old breeds of cattle (Zebu, Guernsey), whereas variant A¹ evolved much later and is characteristic to contemporary breeds (Hanusova et al., 2010). Variant B is less common, and A³ and C exist rarely (Farrell et al., 2004). These alleles are most common for European breeds of cattle.

Allele E was only identified for the Italian Piemontese breed. The occurrence of genetic variants is based on nucleotide substitutions within exon VII (A1, A2, A3 and B) and exon VI (C and E) (Jann et al., 2002). Table 2 shows the frequencies of β -casein alleles in various breeds of cattle.

The κ -CN family consists of a major carbohydrate-free component and a minimum of 6 minor components. The 6 minor components are detected by PAGE in urea with 2-mercaptoethanol. In the basic structure of the reference protein of κ -CN family is a major carbohydrate-free component of κ -CN-1P. It consists of 169 amino acid residues arranged in the following order: Asp₄, Asn₈, Thr₁₅, Ser₁₂, Ser P₁, Pyroglu₁, Glu₁₂, Gln₁₄, Pro₂₀, Gly₂, Ala₁₄, Cys₂, Val₁₁, Met₂, Ile₁₂, Leu₈, Tyr₉, Phe₄, Lys₉, His₃, Trp₁ and Arg₅, with a molecular weight of 19.307 (Farrell et al., 2004). What is more, the length of κ -casein is less than 13 kb, though most of the coding sequences are comprised in the exon IV. κ -casein differs significantly from other caseins, both in terms of properties and structure. It is highly homologous to the fibrinogen gamma chain. What is more it serves a similar function, while being a stabilizing factor during the formation of the clot (Azevedo et al., 2008). So far 12 genetic variants of κ -casein were identified: A, A¹, B, C, E, F¹, F², G¹, G², H, I and J (Chen et al., 2008; Farrell et al., 2004). The differences between them are caused by two point mutations involving a substitution of threonine with isoleucine at the 136 position of polypeptide chain and aspartic acid with alanine at the 148 position (Azevedo et al., 2008). What is more, at the C-terminal part of κ -casein molecule a macropeptide residue can be found (106-169 chain fragment) (Farrell et al., 2004). Numerous studies focused on the analysis of genes that control the frequency of κ -CN polymorphism exhibit a superior frequency of allele A above allele B - for dairy, meat and also high productivity and local breeds (Król, 2003; Tsiaras et al., 2005). Azevedo et al. (2008) in their research on Brazilian cattle stated that the frequency of allele B of κ -casein ranges from 0.01 to 0.30. Kučerova et al. (2006) have also demonstrated a high frequency of allele B (0.38) and genotype BB (13 %) in the population of Czech Fleckvieh cattle. Table 3 shows the frequencies of κ -casein alleles in various breeds of cattle.

Cattle breed	Allelic frequencies of β -casein	References
Holstein-Friesian	$A^1 = 0.472$ $A^2 = 0.496$ $B = 0.026$	Ehrmann et al., 1997
Jersey	$A^1 = 0.093$ $A^2 = 0.721$ $B = 0.186$	
Jersey	$A^1 = 0.123$ $A^2 = 0.591$	Winkelman & Wickham, 1997
Polish Red	$A^1 = 0.617$ $A^2 = 0.321$ $B = 0.062$	Erhardt et al., 1998
Red Danish Dairy Cattle	$A^1 = 0.710$ $A^2 = 0.230$ $B = 0.060$	
German Red	$A^1 = 0.628$ $A^2 = 0.302$ $A^3 = 0.013$ $B = 0.057$	
Estonian Native	$A^1 = 0.318$ $A^2 = 0.644$ $B = 0.038$	Jõuru et al., 2007
Western Finncattle	$A^1 = 0.292$ $A^2 = 0.671$ $B = 0.037$	
Danish Jersey	$A^1 = 0.094$ $A^2 = 0.688$ $B = 0.219$	

Table 2. The frequencies of β -casein alleles in various breeds of cattle

Cattle breed	Allelic frequencies of κ -casein	References
Jersey	$A = 0.110$ $B = 0.880$	Ren et al., 2011
Holstein	$A = 0.690$ $B = 0.310$	
Romanian Spotted	$A = 0.650$ $B = 0.350$	Ilie et al., 2007
Brown of Maramures	$A = 0.375$ $B = 0.625$	

Cattle breed	Allelic frequencies of κ -casein	References
Holstein-Friesian	A = 0.940 B = 0.060	Tsiaras et al., 2005
Holstein	A = 0.760 B = 0.240	Bonvillani et al., 2010
Simmentaler	A = 0.531 B = 0.469	Feleńczak et al., 2008
Polish Red	A = 0.690 B = 0.310	Erhardt et al., 1998
Red Danish Dairy Cattle	A = 0.810 B = 0.190	
German Red	A = 0.642 B = 0.288 E = 0.070	
Hereford and crossbreeding F ₁ and R ₁ (Black and White x Hereford)	A = 0.722 B = 0.277	Litwińczuk & Król, 2002
Limousine and crossbreeding F ₁ and R ₁ (Black and White x Limousine)	A = 0.607 B = 0.393	
Simmentaler	A = 0.681 B = 0.302 E = 0.017	
Estonian Native	A = 0.695 B = 0.305	Jõuru et al., 2007
Western Finncattle	A = 0.671 B = 0.305 E = 0.024	
Danish Jersey	A = 0.512 B = 0.488	
Estonian Holstein	A = 0.790 B = 0.138 E = 0.072	
Estonian Red	A = 0.642 B = 0.324 E = 0.034	

Table 3. The frequencies of κ -casein alleles in various breeds of cattle

β -lactoglobulin is a major whey protein. Bovine BLG gene is located on chromosome 11 (11q28) and is responsible for coding the main whey protein which is β -lactoglobulin. It consists of 7 exons and its length is approximately 6 700 bp.

Cattle breed	Allelic frequencies of β -lactoglobulin	References
Jersey	A = 0.320 B = 0.680	Ren et al., 2011
Holstein	A = 0.320 B = 0.680	
Czech Fleckvieh	A = 0.511 B = 0.489	Kučerova et al., 2006
Holstein-Friesian	A = 0.480 B = 0.520	Tsiaras et al., 2005
Uruguayan Creole	A = 0.4938 B = 0.5062	Rincón et al., 2006
Polish Red	A = 0.188 B = 0.740 C = 0,058 I = 0,014	Erhardt et al., 1998
Red Danish Dairy Cattle	A = 0.110 B = 0.890	
German Red	A = 0.157 B = 0.775 C = 0.068	
Hereford and crossbreeding F ₁ and R ₁ (Black and White x Hereford)	A = 0.278 B = 0.722	Litwińczuk & Król, 2002
Limousine and crossbreeding F ₁ and R ₁ (Black and White x Limousine)	A = 0.520 B = 0.480	
Simmentaler	A = 0.379 B = 0.621	
Estonian Native	A = 0.314 B = 0.686	Jõuru et al., 2007
Western Finncattle	A = 0.098 B = 0.902	
Danish Jersey	A = 0.463 B = 0.537	
Estonian Holstein	A = 0.421 B = 0.579	
Estonian Red	A = 0.254 B = 0.746	

Table 4. The frequencies of β -lactoglobulin alleles in various breeds of cattle

The first who discovered its polymorphism were Aschaffenburg and Drewry in 1955 (as cited in El-Hanafy et al., 2010). So far 12 genetic variants of β -lactoglobulin were identified: A, B, C, D, E, F, G, W, H, I, J and X; they encode different forms of proteins (Farrell et al., 2004). For most cow breeds, both variant A and B are most common and occur with high frequency (Heidari et al., 2009). Mutations in the nucleotide sequence resulting in substituting of amino acids are distributed on 3 exons: exon 2 (allele D), exon 3 (alleles A and B) and exon 4 (alleles A, B and I) (Kamiński, 2001). The differences between variant A and B occur because of the existence of different amino acids at position 64: aspartic acid for variant A and glycine for variant B. What is more, at position 118 variant A has valine and variant B alanine (Kučerova et al., 2006). The presence of one of the variants (A or B) significantly influences the physicochemical properties of milk and also raises the actual contents of β -lactoglobulin (Farrell et al., 2004). Tsiaras et al. (2005) noted the presence of 3 genotypes with the frequencies ranging from 0.25 to 0.47. What is more, Heidari et al. (2009) calculated the frequencies of β -lactoglobulin genotypes at the levels of: 0.257 for AA, 0.544 for AB and 0.198 for BB. Kučerova et al. (2006) observed that the proportion of AB β -lactoglobulin genotype ranged from 49.5 to 66.6 % corresponding to other genotypes: for AA from 18.2 to 26.4 % and for BB from 15.2 to 24.1 %. Table 4 shows the frequencies of β -lactoglobulin alleles in various breeds of cattle.

α -LA gene encoding α -lactalbumin is localized on chromosome 5 (BTA5q12-13). α -lactalbumin has the length of 3 061 bp and it consists of 4 exons. The polymorphism of this gene is revealed in cattle breeds deriving directly from *Bos indicus*. What is more α -lactalbumin appear most commonly in 2 forms: A and B (Kamiński, 2001). In bovine milk the concentration of α -lactalbumin varies between 1.2 and 1.5 g/l (Farrell et al., 2004). This whey protein has a precise role in the mammary gland. It reacts with the enzyme β -1,4-galactosyltransferase to form the lactose synthase complex within the Golgia apparatus. It allows the formation of lactose from glucose and UDP-galactose thank to the modifications in the substrate specificity of β -1,4-galactosyltransferase. The function of lactose as a main osmolyte of milk and its production demonstrate the importance of this fraction (Farrell et al., 2004).

2.2. Goats

Goat milk contains 4 caseins (α ₁-, α ₂-, β - and κ -) linked with each other encoded respectively by autosomal genes: CSN1S1, CSN1S2, CSN2 and CSN3. They are located on chromosome 4 in the following order: α ₁-, β -, α ₂- and κ -. The CSN1S1 gene encoding α ₁-casein has the most complex construction and has a number of polymorphic sites. It has the size of 16.7 kb and it consists of 19 exons with a length of 24 to 385 bp and 18 introns with a length of 90 to 1 685 bp (Supakorn, 2009).

The gene CSN1S1 in goats presents the highest level of variability of all the casein genes among all species of ruminants that have been analysed. So far 16 genetic variants of α ₁-casein were identified: A¹, B¹, B², B³, B⁴, C, E, F, G, H, I, L, M, N, O¹ and O². They probably evolved from 4 original alleles: A, B¹, B² and W. What is more, these different alleles are

associated with 4 levels of protein synthesis in milk. A high level of α_1 -casein (3.5-3.6 g/l) synthesis is connected with "strong" alleles: A, B¹, B², B³, B⁴, C, H and L. "Medium" alleles determine the protein synthesis at the levels of 1.1-1.6 g/l, while "weak" alleles are associated with the synthesis only at the amounts of 0.45-0.6 g/l. "Null" alleles (0¹ and 0²) account for trace amounts or complete absence of this casein fraction in milk (Caravaca et al., 2008; Ibeagha-Awemu et al., 2005; Moatsu et al., 2006; Veress et al., 2004). Table 5 shows the frequencies of α_1 -casein alleles in various breeds of goats.

In the local breeds of goats the frequency of A, B and C alleles (so called "strong" alleles) is generally higher, whereas in typical dairy breeds the frequency of so called "medium" and "weak" alleles exceeds (Barłowska et al., 2007a; Jordana et al., 1996; Torres-Vázquez et al., 2008). Moatsou et al. (2008) analysed the contribution of individual genetic variants of α_1 -casein in goats of local Greek and international breeds (Alpine and Saanen). In their research they presented that in local breeds of goats "strong" alleles exceeded and there were no "weak" and "null" alleles. In the international breeds, however, "medium" variants were in majority, and nearly 1/3 had "weak" and "null" alleles. Table 5 shows the frequencies of α_1 -casein alleles in various goat breeds.

Goat's CSN1S2 locus is characterized by a much higher genetic diversity compared to cattle or sheep. So far 8 alleles associated with different level of synthesis of α_2 -casein have been identified: alleles A, B, C, E and F are the so called "normal" alleles connected with the synthesis of α_2 -casein at the level of 2.5 g/l; allele D is an intermediate allele associated with the synthesis of α_2 -casein at the level of 1.25 g/l; "null" alleles linked to the absence or synthesis of α_2 -casein at trace levels. Chessa et al. (2003) presented in their research that the population of Italian dairy goats (Maltese breed) are characterized by the presence of 5 alleles of CSN1S2: A, B, C, G and 0 with the frequencies: 0.548, 0.062, 0.319, 0.067 and 0.005 respectively.

So far 5 alleles of goat's CSN2 gene were identified that are associated with different levels of β -casein in milk. Alleles A, B and C are connected with normal contents of this protein, while alleles 0 and 0' are linked with undetectable or trace amounts (Ibeagha-Awemu et al., 2005). Sztankóová et al. (2005) in goats from two local breeds White Short-Haired (WSH) and Brown Short-Haired (BSH) maintained in Czech Republic identified allele A associated with "normal" synthesis of β -casein and allele 0 connected with a lack of synthesis of β -casein. Goats in the studied population, however, were not associated with a variant 0 of CSN2.

Goat κ -casein gene is composed of 5 exons, out of which the portion encoding the mature protein is located in the exon 3 (9 amino acids) and exon 4 (162 amino acids). It is assumed that the κ -casein gene is not evolutionary correlated to milk proteins sensitive to calcium, although it is linked with them. There is a hypothesis that it is related to the fibrinogen (Strzelec & Niznikowski, 2009). CSN3 was not considered a multiallelic gene until 1990, when Di Luccia et al. (1990) reported variability (alleles A and B) in an unspecified Italian breed. Since then, 11 following variants of this protein were identified: C, D, E, F, G, H, I, J, K, L and M (Ibeagha-Awemu et al., 2005). Chessa et al. (2003) in the Maltese goat breed

Breed	Country	Allel								References
		A	B	C	D	N	E	F	D+O	
Toggenburg	Mexico	0.141	0.212			0.179	0.147	0.321		Torres-Vázquez et al., 2008
Appearance of Murciana-Granadina	Mexico	0.250	0.135			0.058	0.442	0.115		
Mosaico Lagunero	Mexico	0.183	0.350			0.183	0.050	0.233		
Saanen	Mexico	0.031	0.108			0.072	0.418	0.371		
Alpine	Mexico	0.185	0.142			0.154	0.241	0.278		
Alpine	Spanish	0.14	0.05	0.01	0.34			0.41	0.05	Jordana et al., 1996
Murciano-Granadina	Spanish	0.08	0.23		0.59			0.08	0.02	
Malagueña	Spanish	0.09	0.09		0.65			0.04	0.13	
Payoya	Spanish	0.05	0.19		0.76					
Canaria	Spanish	0.28	0.32		0.20				0.20	
Palmera	Spanish	0.68	0.23		0.09					
Majorera	Spanish	0.07	0.38		0.24				0.31	
Tinerfeña	Spanish	0.15	0.35		0.32				0.18	
Boer	Malaysia	0.15	0.10	0.71				0.04		Marini et al., 2011
Boer-Feral	Malaysia	0.22		0.68				0.03		
Katjang	Malaysia	0.61	0.11	0.17						
Jamnapari	Malaysia	0.51	0.10	0.28				0.10		
White improved	Poland	0.252	0.285				0.463			Barłowska et al., 2007a
Colored improved	Poland	0.194	0.319				0.487			
White non-improved	Poland	0.185	0.233				0.582			
Colored non-improved	Poland	0.182	0.196				0.622			

Table 5. The frequencies of α s₁-casein alleles in various breeds of goats

characterized 3 alleles of CSN3, i.e. A, B and D with the frequency: 0.089, 0.230 and 0.708 respectively. Sztankóová et al. (2005) in White Short-Haired (WSH) and Brown Short-Haired (BSH) breeds of goats also identified 3 alleles of CSN3, although these were alleles A, B and C. The frequencies of A, B and C alleles were, respectively: 0.15, 0.80 and 0.05 for the WSH breed and 0.52, 0.40 and 0.03 for BSH breed. Bemji et al. (2006) in Nigerian Red Sokoto breed characterized the presence of 3 alleles of CSN3, i.e. A, B and M with the following frequencies: 0.453, 0.523 and 0.023.

Breed	-60C allele	-60T allele	References
Muriciano Grandana	0.86	0.14	Yahyaoui et al., 2000
Canaria	1	-	
Payoya	0.73	0.27	
Malguena	0.75	0.25	
Saanen	0.73	0.27	
Hungarian Milk	0.88	0.12	Veress et al., 2004

Table 6. The frequencies of β -lactoglobulin in various breeds of goats

Goat's LAA and LBG genes encoding 2 major whey proteins, respectively, α -lactalbumin and β -lactoglobulin, are characterized with much lower genetic variation in comparison to the genes observed in cattle. Goat's LGB gene is located on chromosome 11q28. What is more there is a high homogeneity of β -lactoglobulin in bovine, ovine and goat (at the level of 95 %). Sheep and goat β -lactoglobulin differs itself from bovine β -lactoglobulin only in 6 positions (Strzelec & Niznikowski, 2009; Yahyaoui et al., 2000). Table 6 shows the frequencies of β -lactoglobulin in various breeds of goats.

2.3. Sheep

The research on the analysis of milk protein polymorphism in sheep is limited to the study of the gene polymorphism of α ₁-casein and β -lactoglobulin.

BLG gene in sheep is located on chromosome 3 and three alleles can be found within its area: A, B and C. Alleles A and B (present in all breeds) differ in the substitution of 1 amino acid at position 20 of the polypeptide chain, i.e. for variant A it is tyrosine, while for variant B it is histidine. Variant C of β -lactoglobulin, which is rare, is a subtype of allele A and it was recognized within the German and Spanish Merino breed. It differs from variant A with a substitution of arginine with glutathione at position 148 of the amino acid chain (Arora et al., 2010; El-Shazly et al., 2012; Mohammadi et al., 2006).

Sheep milk contains 4 casein fractions: α ₁- α ₂- β - and κ - encoded by the genes: CSN1S1, CSN1S2, CSN2 and CSN3. These genes are localized on chromosome 4. So far 8 alleles of CSN1S1 were identified: A, B, C, D, E, F, G and H (Giambra et al., 2010). Vlaic et al. (2011) evaluating 282 sheep from 5 breeds maintained in Romania: Turcana, Carabasa, Tigaie (white and rusty varieties), Cluj Merinos, Botosani Karakul (black, dark grey, brown, light grey, pink and white varieties) have reported the presence of 2 alleles of BLG, i.e. A and B. The frequencies of alleles ranged: for allele A from 0.422 to 0.800 and for allele B from 0.133 to 0.578. Mroczkowski et al. (2004) in Polish Merino identified: 4 alleles of CSN1S1 (A, B, C and D), 3 alleles for CSN2 (A, B and C) and 2 alleles for β -lactoglobulin (A and B). They indicated the existence of alleles, respectively: for α -lactalbumin only 1 allele A with a frequency of 1.00; for α ₁-casein 4 alleles with frequencies of A=0.078, B=0.007, C=0.905 and D=0.010; for β -casein 3 alleles with frequencies of A=0.944, B=0.051 and C=0.005; for β -lactoglobulin 2 alleles with frequencies of A=0.498 and B=0.502.

2.4. Buffalo

Buffalo milk is characterized by the presence of all 4 casein fractions (α_1 -, β -, α_2 - and κ -) encoded by 4 closely linked autosomal genes (CSN1S1, CSN2, CSN1S2 and CSN3) that are mapped on chromosome 7 (Iannuzzi et al., 2003). These casein fractions are distributed in buffalo milk respectively: β - (53.45 %), α_1 - (20.61 %), α_2 - (14.28 %) and κ - (11.66 %) (Cosenza et al., 2011). What is more, BLG gene is mapped on chromosome 12 (as cited in El Nahas et al., 2001). Ren et al. (2011) assessing the population of 48 water buffaloes identified only the existence of allele B of CSN3 and LBG. Allele A was not present at all for these fractions of protein. Similar results were established by Shende et al. (2009) who were studying the polymorphism of κ -casein in 20 buffaloes – only allele B of CSN3 was identified.

3. Milk protein genes as markers of production traits

The research on determining the relationship between the presence of different genetic markers and production traits of animals is being conducted for many years now. In the livestock farming the emphasis was put on milk protein genes.

3.1. The association between selected genetic variants with the chemical composition of milk

3.1.1. Cattle

A major milk protein which is considered to be an important genetic marker of quantitative traits is β -lactoglobulin. Analysing the association of genetic variants of β -lactoglobulin with the chemical composition of milk, most authors link the variant B of β -lactoglobulin with the higher contents of total protein, casein, fat and dry matter in milk (Barłowska, 2007; Barłowska et al., 2007b; Ng-Kwai-Hang, 2002). Lodes et al. (1997) presented in their research that the gene B of β -lactoglobulin led to the increase of total protein in milk (including casein) with the simultaneous decrease of contents of whey proteins. The protein contents, depending on the genotype of β -lactoglobulin was reduced, respectively: for total protein – BC>AD/BB>AB>AA/BD; for casein – BC>BB>AD/AB/BD>AA; for whey protein – AA>AD>AB>BC>BD>BB. A similar relationship was ascertained by Bonfatti et al. (2010) who conducted research on 2 167 cows of the Simmental breed maintained in 47 herds in Northern Italy. They have also reported the positive influence of allele B of β -lactoglobulin on the percentage contribution of all casein fractions and α -lactalbumin and negative effect on the contents of β -lactoglobulin. Contrary to that research, Hallen et al. (2008) presented a negative association of variant B of β -lactoglobulin with the concentration of total protein.

Ryniewicz et al. (1998) in their research showed that the physical structure, i.e. the compactness of the casein curd connected with the ease and speed of its digestion, is associated with the polymorphic forms of milk proteins. What is more, milk with AB heterozygotes of β -lactoglobulin has the most digestible protein which may be associated

with better results of rearing of offspring from cows with this genotype. This fact is confirmed by the studies of Litwińczuk & Król (2002) and Król (2003) who evaluated the cows of the Limousine and Hereford breeds; the research focused on calves to the age of approximately 8 months. The average daily gains of calves reared by cows of the Hereford breed with AB genotype of β -lactoglobulin (861.3 g) were 115.7 g higher in comparison to the increments of calves reared by cows with AA genotype and 33 g higher compared to BB homozygotes of β -lactoglobulin. Higher daily gain of calves with AB genotype of β -lactoglobulin led to higher body weight at the age of 210 days (207.4 kg) in comparison to BB (192.7 kg) and AA (184.1 kg) homozygotes. Similar results were presented in Henderson & Marshall (1996) studies on the multi-breed population of beef cattle. They stated that the best results of rearing calves were achieved by cows with the AB and BB genotypes of β -lactoglobulin.

A milk protein which arouses the greatest interest as a genetic marker is κ -casein. On the one hand (Barłowska et al., 2007b; Litwińczuk et al., 2006; Winkelman & Wickham, 1997) in their studies link AA genotype of κ -casein with a higher yield of milk. On the other hand Creamer & Harris (1997) present that the highest daily yield of milk is obtained from cows with AB genotype of κ -casein. Król (2003) who conducted research on beef cattle of the Hereford breed has also concluded that the highest milk yield was associated with the AB genotype of κ -casein. Henderson & Marshall (1996), who analysed the characteristics of milk yield in the multi-breed population of beef cattle in South Dakota, stated that the cows with AB and AA genotypes of κ -casein produced the most milk and BB homozygotes of κ -casein the lowest quantity. Lodes et al. (1997) within 7 genotypes of κ -casein, i.e. AA, AB, AC, AE, BB, BC and BE did not describe significant differences in the productivity of dairy cows. Some authors point to a higher concentration of total protein (including casein) and fat in milk from cows of BB homozygotes of κ -casein (Barłowska, 2007; Karima et al., 2010). Henderson & Marshall (1996) also indicate the relationship between genetic variants of κ -casein with the results of rearing calves.

The progeny of cows with AB genotype of κ -casein achieved the highest daily gain (932 g) and the highest body weight at the peak (242 kg). Similar results were presented in the research of Król (2003) who carried it out on cows of the Hereford and Limousine breed.

In most studies focused on the analysis of genotype of α_{S1} -casein and β -casein no clear significant relation of these genetic variants on cow productivity (and contents of protein and casein in milk) was presented (Huang et al., 2012; Ikonen et al., 2001; Litwińczuk & Król, 2002). Only the variant C of α_{S1} -casein is associated with a slightly higher contents of protein and casein in milk in comparison to allele B of α_{S1} -casein (Winkelman & Wickham, 1997). McLean (1984) indicates the connection of variant C of α_{S1} -casein with a higher concentration of α_{S1} -casein and also with a simultaneous decrease of κ -casein in milk.

In the case of β -casein the research is mainly focused on the subfraction A of β -casein, i.e. A¹, A², A³. Most studies (Nilsen et al., 2009; Olenski et al., 2010; Winkelman & Wickham, 1997) indicate the positive association of variant A² of β -casein on milk yield and the contents of protein. According to Nilsen et al. (2009) and Olenski et al. (2010) A² allele of β -casein is an

effective genetic marker for the productivity of proteins. They suggest conducting a selection of cattle to raise its frequency. Table 7 shows the association of genetic variants of cattle milk proteins with milk yield and its composition.

Item	Protein fraction		
	β -LG	κ -CN	α_{S1} -CN
Milk yield	AA>BB>AB (Creamer & Harris, 1997; Walawski et al., 1994) AB>AA>BB (Henderson & Marshall, 1996; Król, 2003)	AB>AA>BB (Creamer & Harris, 1997; Henderson & Marshall, 1996; Król, 2003) AA>AB>BB (Litwińczuk et al., 2006)	no distinct tendency between genotypes
Total protein	BB>AB>AA (Lunden et al., 1997; Ng-Kwai-Hang, 2002) AA/AB>BB (Creamer & Harris, 1997; Hallen et al., 2008)	BB>AB>AA (Barłowska et al., 2007b; Creamer & Harris, 1997; Feleniczak et al., 2004, Karima et al., 2010)	CC/BC>BB (Winkelman & Wickham, 1997)
Casein	BB>AB>AA (Bonfatti et al., 2010, Creamer & Harris, 1997; Heck et al., 2009)	BB>AB>AA (Creamer & Harris, 1997; Feleniczak et al., 2004, Karima et al., 2010)	CC/BC>BB (Winkelman & Wickham, 1997)
Whey protein	AA>AB>BB (Creamer & Harris, 1997; Lunden et al., 1997)	AA>AB>BB (Creamer & Harris, 1997)	AB>BB>BC (Creamer & Harris, 1997)
Fat	BB>AB>AA (Ng-Kwai-Hang, 2002)	BB>AB>AA (Barłowska et al., 2007b; Karima et al., 2010)	no distinct tendency between genotypes

Table 7. The association of genetic variants of cattle milk proteins with milk yield and its composition

3.1.2. Goats

From all polymorphic proteins in goats the most known is definitely α_{S1} -casein. In most studies, no significant correlation between the variants of α_{S1} -casein and milk productivity was ascertained linking this with a strong influence of various factors such as age, stage of lactation etc. (Barłowska et al., 2007a; Litwińczuk et al., 2007; Remeuf, 1993). Some authors, however (Ryniewicz et al., 2000; Vassal & Manfredi, 1994), indicate a lower daily milk yield from goats with a variant E of α_{S1} -casein. Most of the studies on goat milk were focused on the analysis of the association of polymorphic variants of α_{S1} -casein with the chemical composition of milk and its technological properties (Barłowska et al., 2007a; Clark & Sherbon, 2000; Remeuf, 1993; Schmidely et al., 2002). A positive influence of “strong”

variants (A, B and C) of α_{S1} -casein on the concentration of particular milk components (especially proteins) was demonstrated (Barłowska et al., 2007a; Krzyżewski et al., 2000; Litwińczuk et al., 2004; 2007b; Remeuf, 1993; Schmidely et al., 2002; Vassal & Manfredi, 1994). Krzyżewski et al. (2000) analysing the population of White improved breed of goats indicated a higher contents of protein (about 0.15 % more) in the milk of goats characterized by “strong” polymorphic variants of α_{S1} -casein in comparison to animals with “medium” variants. In the studies conducted by Litwińczuk et al. (2004) on goats originating from the region of Wielkopolska and Podkarpacie differences in total protein contents between goats with “strong” and “medium” variants ranged from 0.29 to 0.39 %. Schmidely et al. (2002) compared the chemical composition of homozygotes AA and FF of α_{S1} -casein of the Alpine and Sannen breeds and showed that the animals with AA genotype produced milk with a higher contents of fat (about 1.2 g/kg more) and protein (about 6.3 g/kg more) in comparison to goats with FF homozygotes.

A propitious relationship between “strong” α_{S1} -casein genotypes and contents of fat and protein in milk was also described in the research of Barłowska et al. (2007a and 2007c) conducted on goats of 4 breeds. Moreover, a clear association of α_{S1} -casein genotypes with the concentration of casein was indicated. In a group of goats with the highest contents of casein in milk (≥ 2.4 %) in each breed goats with “strong” genotypes (AA, AB, BB, AE and BE) were predominant – in comparison to animals with “medium” genotypes the prevalence ranged from 7.2 % (for coloured non-improved breed) to 29.1 % (for white improved breed of goats). The opposite situation was observed for samples containing the lowest amounts of casein (≤ 1.99 %). In every breed goats with “medium” genotypes of α_{S1} -casein dominated. Their prevalence ranged from 7.9 % for white non-improved breed to 19.0 % for coloured improved breed. According to Vassal & Manfredi (1994) the contents of casein in milk depending on the different alleles of α_{S1} -casein varies, respectively: for “strong” alleles, i.e. A, B and C- 3.6 g/l; for “medium” alleles, i.e. E and G – 1.6 g/l; for “weak” alleles, i.e. D and F – approximately 0.6 g/l. The presence of “null” variant is related to the synthesis of trace amounts or the complete absence of this fraction.

Genetic variants of α_{S1} -casein are not only associated with the protein contents in milk but also with their quantitative proportions both within α_{S1} -casein and the rest of proteins from casein group. What is more, milk from goats with “strong” alleles of α_{S1} -casein contains more Ca and Zn (Krzyżewski et al., 2002).

Ryniewicz et al. (1998) also presented a relationship between polymorphic variants of α_{S1} -casein and susceptibility of total protein to hydrolysis. Significantly higher degree of hydrolysis of protein was determined in the milk of goats characterized by “weak” variants of α_{S1} -casein.

3.1.3. Sheep

Most studies conducted on ovine milk concern the association of polymorphic variants of α_{S1} -casein, β -casein and β -lactoglobulin on the chemical composition of milk. It was

indicated that sheep with CC genotype of α_{S1} -casein are characterized by a higher contents of base composition. In the studies conducted on the population of the Polish Merino and Polish Merino x Prolific sheep (Mroczkowski et al., 2002) it was determined that milk obtained from CC homozygotes of α_{S1} -casein contained significantly more protein and dry matter in comparison to AC and BC heterozygotes. What is more, BC genotype of α_{S1} -casein was associated with a higher milk production.

There are not many studies concerning the relationship between polymorphic variants of β -casein and the composition of milk. In the research of Mroczkowski et al. (2004) sheep with AA genotype of β -casein were characterized by a higher contents of protein and dry matter in comparison to individuals with AB genotype of β -casein. However, AB heterozygotes of β -casein corresponded to a higher milk production.

The results of Mroczkowski et al. (2004) indicate that the AA and BB homozygotes of β -lactoglobulin were characterized by higher yields of milk and contents of protein and casein than AB heterozygotes. In the research of Nudda et al. (2000) who analysed the milk of Sarda sheep, it was stated that the genetic variants of β -lactoglobulin have an association with only the milk yield, i.e. animals with AB genotype of β -lactoglobulin were considered to have the highest daily production. The results of other authors are presented in the Table 8.

Item	Protein fraction	
	β -LG	α_{S1} -CN
Milk yield	AA/BB>AB (Mroczkowski et al., 2004) AB>AA>BB (Nudda et al., 2000)	BC>CC>CD (Chianesse et al., 1996) BC>AC>CC (Mroczkowski et al., 2002)
Total protein	BB>AB >AA (Krukovics et al., 1998; Mroczkowski et al., 2002)	CC>CD>BC (Chianesse et al., 1996) CC>AC>BC (Mroczkowski et al., 2002)
Casein	BB>AB>AA (Krukovics et al., 1998)	CC>CD>BC (Chianesse et al., 1996)
Fat	no distinct tendency between genotypes	CC>AC>BC (Mroczkowski et al., 2002; Mroczkowski et al., 2004)

Table 8. The association of genetic variants of ovine milk proteins with the milk yield and chemical composition

3.2. The association between selected genetic variants with the parameters of technological suitability of milk

3.2.1. Cattle

For cattle, polymorphic forms of κ -casein and β -lactoglobulin are strongly associated with the parameters of technological suitability of milk.

Many studies emphasize the distinct association of genetic variants of β -lactoglobulin with the chemical composition of milk and cheese yield. Most of the authors combine BB variant of β -lactoglobulin with the higher contents of fat in milk (Bałowska, 2007; Bałowska et al.,

2007b; Ng-Kwai-Hang, 1997), protein (Ng-Kwai-Hang, 2002), casein (Lunden et al., 1997), dry matter and also with the higher cheese yield as well as better thermal stability of milk (Imafidon & Ng-Kwai-Hang, 1991). Lodes et al. (1997) analysing the chemical composition of milk obtained from 801 cows demonstrated that among 7 genotypes of β -lactoglobulin the highest protein contents was associated with animals with BC (3.76 %) genotype of β -lactoglobulin, and the highest casein contents with BC (2.97 %) and BB (2.85 %) genotypes of β -lactoglobulin. What is more, BW genotype of β -lactoglobulin was characterized with the lowest amount of protein (3.44 %) and casein (2.68 %). In their research Vătăşescu-Balcan et al. (2007) presented that the BB homozygotes of β -lactoglobulin are associated with the production of milk rich in fat and protein and therefore very valuable in the manufacture of cheese. According to Creamer & Harris (1997) variant A of β -lactoglobulin contributes (in contrary to variant B) to the formation of more concise clot at approximate pH of 7. Variant B, in turn, is associated with faster thermal coagulation of milk. Imfidon & Ng-Kwai-Hang (1991) also claim that the milk obtained from cows with AA genotype of β -lactoglobulin is more resistant to high temperatures. In studies of Barłowska (2007) it was presented that the best properties in terms of contents of protein (including casein), fat and dry matter was found in milk obtained from cows with genotypes AA or AB of β -lactoglobulin (which means that the variant A was present). Milk from cows with BB genotype of β -lactoglobulin indicated the shortest ($p \leq 0.05$) time of rennet coagulation. However, milk from animals with heterozygotes (β -LG AB) was characterized by the longest heat treatment stability, i.e. about 29 s longer related to AA homozygotes of β -lactoglobulin ($p \leq 0.05$). A more explicit studies are formulated by authors presenting an association of genetic variants of κ -casein with milk composition and its suitability for cheese production. Most of them (Azevedo et al., 2008; Felańczak et al., 2004; FitzGerald, 1996; Imafidon & Ng-Kwai-Hang, 1991; Lunden et al., 1997; Tsiaras et al., 2005) indicate the fact that cows with BB genotype of κ -casein produce milk with a higher contents of total protein and casein. In addition, this genotype increases the fat contents in milk, provides better stability of casein micelles, shorter time of flocculation, firmer clot formation and higher cheese yield. So that, it can be concluded that genes coding the synthesis of κ -casein have an influence on technological processes in cheese-making. Barłowska et al. (2007b) stated in their research that the presence of B variant of κ -casein in cows (of the Polish Red and White-back breed) favourably affects the contents of dry matter, total protein, casein and also it reduces the time of enzymatic coagulation and prolongs the colloidal stability of milk. According to Robitaille et al. (2001) the genetic polymorphism in the gene expression of κ -casein may influence the physicochemical properties of casein micelles (it is a component stabilizing micelles) and thus the technological properties of milk. What is more, BB genotype not only affects the increase of stability of casein micelles but also quantities of casein (in which it increases the contents of κ -casein fraction within all caseins). FitzGerald (1996) in his research presented that from milk with BB genotype of κ -casein it is possible to achieve higher yields of cheese (Edam, Gouda, Cheddar, Mozzarella). This may be associated with a higher fat recovery from cheeses manufactured from that milk. In the research of Imafidon & Ng-Kwai-Hang (1991) it was presented that milk with BB genotype of κ -casein is more resistant to heat treatment.

Four casein *loci* (CSN1S1, CSN2, CSN1S2 and CSN3) are closely linked and conduct as one genetic unit, thus form different combinations of alleles (haplotypes). According to Matajicek et al. (2007) 15 combinations of κ -casein and β -lactoglobulin were identified and the most frequent were AB/AB (21.0 %) and AA/AB (18.3 %). What is more, BB/AA genotype was determined to have the highest positive association with the evaluated properties of milk. AB/BB, BB/BB, BB/AB and AB/AB genotypes also had a positive correlation with the quality of milk and its clotting properties, whereas genotypes with allele E of κ -casein negatively affected these parameters. It was presented that the distribution of allele A in the combination of κ -casein and β -lactoglobulin genotypes resulted in the increase of milk yield, while the presence of allele B was associated with increased contents of protein and fat in milk. Comin et al. (2008) indicated that κ -casein and β -lactoglobulin genotypes had a strong relationship with parameters of milk coagulation but not with fat and protein contents and other parameters of milk quality. The best results affecting the clotting of milk were these combinations of κ -casein and β -lactoglobulin that contained at least 1 allele B in both *loci*. κ -casein *locus* was more strongly associated with milk coagulation parameters, whereas β -lactoglobulin was more connected with milk yield and proteins.

3.2.2. Goats

Many studies (Barłowska et al., 2007a,c; Devold et al., 2010; Remeuf, 1993; Mahé et al., 1994; Strzałkowska et al., 2004) indicate a strong relationship between genetic variants of CSN1S1 with the chemical composition of milk, mainly the contents of casein, but also with its technological parameters important for cheese production. Homozygous goats with “strong” alleles of CSN1S1 produce milk with significantly higher percentage of protein, fat, calcium and a small diameter of casein micelles. It is possible to acquire more cheese from this type of milk and the curd is more concise in comparison to milk obtained from homozygous goats with “medium” and “weak” alleles. Sacchi et al. (2005) reported that goats with “strong” alleles of α ₁-casein (A, B¹, B², B³, B⁴, C, H, L, M) synthesize this protein fraction on the level of 3.5 g/l of milk. For “medium” (E, J) alleles this value is lower and reaches the level of 1.1 g/l of milk and for “weak” alleles (F, G) it is close to 0.45 g/l of milk. In the case of “null” alleles (0¹, 0², N) this protein is not synthesized. This fact is explained by morphological observations at a cellular level of mammary tissue performed by Martin et al. (1999). It was reported that epithelial cells of homozygous goats with “weak” alleles of α ₁-casein (E, F, G and O) were characterized by a dramatic swelling of the rough endoplasmic reticulum mainly due to the accumulation of proteins, what strongly suggests a dysfunction in secretion mechanisms. In similar studies Barłowska et al. (2007a) indicated that a group of animals produced milk with the highest contents of casein (over 2.4 %) and protein (over 3.0 %) and individuals with “strong” α ₁-casein variants were predominant. They constituted approximately 70 % (as for protein) and over 85 % in a group of goats which milk was associated with the highest casein level. A contrary tendency was observed in a group of goats producing milk with low protein (≤ 2.4 %) and casein (≤ 2.0 %) contents. There, the individuals with “medium” α ₁-casein genotypes (57 – 59 %) predominated. According to

Pierre et al. (1996) goat milk with AA genotype of α_1 -casein indicated a higher contents of total nitrogen and fat compared to milk obtained from goats with 00 genotype. Cheeses of this type of milk were also more firm, had a higher yield and contained less volatile aromatic compounds. In the research of Clark & Sherbon (2000) it was presented that the milk obtained from goats with at least 1 "strong" (B^1 , B^2 , B^3 or C) genetic variant of α_1 -casein contained more dry matter, SNF, protein and α_1 -casein compared to the milk of goats with "weak" variants of α_1 -casein (F or D) or homozygotes with "null" variants of α_1 -casein (00). However, genetic variants of α_1 -casein were not closely correlated with milk coagulation properties. According to Pop et al. (2008) formation of the characteristic "goat flavour" is also associated with the genotype of α_1 -casein (CSN1S1). Cheese manufactured from milk with AA genotype has a weaker "goat flavour" compared to the one produced from milk with FF genotype. This is explained by the fact that goat milk with FF genotype of CSN1S1 has a higher lipase activity in comparison to milk obtained from goats with AA genotype. There is relatively little research that clarifies the relationship of genetic variants of κ -casein with the technological parameters of goat milk. According to Chiatti et al. (2007) genetic variants of κ -casein may have an association with the contents of protein in milk (including casein) in the following trend: BB>AB>AA.

3.2.3. Sheep

There is not much research explaining the relationship of genetic variants of ovine milk proteins with the technological parameters of milk. Only in a few studies the correlation between β -lactoglobulin variants and base chemical composition was demonstrated. Çelük & Zdemür (2006) evaluating the Awassi and Morkaraman breeds demonstrated that genetic variants of β -lactoglobulin were only associated with the contents of protein and fat in the milk of Awassi sheep, but had no relation to the contents of dry matter, acidity and milk coagulation time in 2 breeds of sheep.

4. The modification of milk composition through genetic engineering

The measures to modify the chemical composition of milk in order to achieve the desired health benefits or processing properties are of increasing importance in dairy biotechnology. The mammary gland is a bioreactor which allows manufacturing of proteins of foreign species. One of the possible changes in the milk composition is the introduction of new or the development of existing milk protein genes which may increase the nutritional value of the product or improve its properties as a raw material for processing (for example by genetic modification of milk it is possible to increase the heat resistance). It is also possible to use the process of "humanization" of cow's milk by the partial replacement of the cattle proteins with those of a human. An important modification of milk is a reduction of lactose contents which adversely affects the quality of cheeses and other dairy products and is not well tolerated by many people as a food ingredient. The decrease of lactose contents in milk may be achieved by inactivating or reducing the expression of α -lactalbumin gene or by introducing active in the mammary gland lactase gene or bacterial β -galactosidase gene

(*lacZ* gene). Studies are also conducted towards reducing or eliminating the contents of the main allergen of cow milk, which is β -lactoglobulin, through the inhibition of expression of BLG gene (*knock-out*). This protein is not present in human milk (Charon & Świtoński, 2000). The progress in the identification of genetic engineering methods utilized in dairy biotechnology will depend, in the near future, not only on the development of molecular biology but mainly on the social acceptance of the research in this area.

5. Conclusion

The extensive use of the achievements of biological and zootechnical sciences in the second half of twentieth century made it possible to attain a significant increase in the productivity of animals. What is more, the wide and easy access to molecular technologies has influenced the evaluation of animals in a way that the practical use of polymorphism of genes as markers of functional traits is commonly utilized. One of such examples is the polymorphism of milk proteins. The available bibliography suggests that these issues were analysed in all four main species of animals determining the global production of milk, i.e. in cattle, buffaloes, goats and sheep, though the cattle have been examined to the greatest extent.

The milk protein of greatest interest as a genetic marker in cattle is the κ -casein, whereas in goats it is α ₁-casein. Based on the results of many studies it is assumed that AA genotype of κ -casein is associated with higher milk production, while the BB genotype with higher contents of base chemical composition (proteins, including casein and fat). This genotype is also related to higher stability of casein micelles, shorter flocculation, firmer clot formation and consequently with a better performance of cheese. In the case of goats, a positive association between variants of “strong” (A, B, C) alleles of α ₁-casein with the composition of milk was demonstrated. Homozygous goats with “strong” alleles of CSN1S1 produced milk with higher contents of proteins, calcium, fat and with a smaller diameter of casein micelles. From the milk of these goats it is possible to obtain more cheese and the curd is more firm in comparison to homozygous goats with “medium” and “weak” alleles of α ₁-casein. Similar dependences were not observed in sheep and buffaloes, perhaps because of the lack of research in that area.

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