



A1 AND A2 MILK & ITS IMPACT ON HUMAN HEALTH

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ABSTRACT

Most common economically important milk constituents traits include fat, protein, SNF, lactose and ash. These characteristics and associated benefits have made milk an important part of the diet. Amongst the milk constituents, beta-casein has gained importance and popularity amongst the health conscious people due to its recent health related issues. Beta casein composition of milk and milk products has become an important economic trait of dairy animals. Our indigenous dairy animals produce A2 milk and India is endowed with rich A2 dairy animals since our civilizations, protecting the masses from ill effects of A1 milk. It is a matter of great concern for the health of people in India. There is a urgent need to go through our breeding policies to stop producing A1 milk.

KEYWORDS: A1 and A2 Milk, Human health**INTRODUCTION**

Milk is the complete food for the infant. It contains the essential micro-nutrients needed for growth and development of human health as well as for the neonate animal. In USA, Australia, New Zealand and other developed countries, people use to consume milk according to their needs and use milk like A2 milk, since A2 milk is harmless whereas A1 milk is harmful for health. So, our future breeding policies for dairy animals should be done in a systematic manner, keeping an eye on producing clean and healthy milk which is none other than A2 Milk.

What actually is A1 and A2 milk?

Milk contains about 85% water. The remaining 15% is the milk sugar lactose, protein, fat and minerals. Beta-casein is about 30% of the total protein content in milk. A2 milk is the milk that contains only the A2 type of beta-casein protein whereas A1 milk contains only A1 beta casein or A1A2 type variant. A1 protein variant is commonly found in milk from crossbred and European breeds of cattle. A2 milk is found basically in indigenous cows and buffaloes of India (Asia as a whole). A2 milk is branded by the A2 Milk Company like A2 Corporation and sold mostly in Australia, New Zealand, United Kingdom and other developed countries.

History of A1 and A2 Milk

A2 beta-casein is the beta-casein from cows that have been produced since before they were first domesticated over 10,000 years ago. It has no known negative effects on human health. In the past few thousand years, a natural mutation occurred which has resulted in a proportion of cows of European breeds producing a casein variant called A1 beta-casein. Slowly, these protein variant became dominant in milk which producing A1 milk. The gene

encoding beta-casein was changed such that the 67th amino acid in the 209 amino proteins was switched from proline to histidine. This new kind of beta-casein that was created is known as A1 beta-casein which is found in the milk of many crossbred cows such as Holstein, jersey and Friesian.

Basic genetics of A1 and A2 milk

The A1/A2 status of a cow is determined by a pair of genes on the sixth chromosome (Rijnkels, 2002). There are two major alleles of the gene i.e A1 and A2 beta-casein alleles. A cow carries two copies of the beta-casein gene; she can carry either of A2A2 (homozygous), A1A2 (heterozygous) or A1A1 (homozygous) alleles. Neither allele is dominant over the other rather; they are co-dominant i.e. additive in their effect. Therefore, an A1A2 cow will produce A1 and A2 beta-casein in equal amounts. An A2A2 cow will only produce A2 beta-casein and an A1A1 cow will only produce A1 beta-casein. The Northern European breeds of cows such as the Friesian and Holstein carry the A1 and A2 allele at about equal levels. The Southern European breeds and the Jersey carry the A1 allele at about 35% and 2/3 of A2. Exceptionally, Guernsey breed appears to carry the A1 allele at less than 10% and the Scottish Ayrshire breed appears to be well over 50%. In addition, individual herds may carry the allele at levels that are quite different to the average for the breed. If a cow is A2A2 then she is guaranteed to pass on the A2 allele to her progeny. Similarly, an A1 cow is guaranteed to pass on the A1 allele. For an A1A2 cow there is a 50% chance of passing on either of the allele.

Status of Milk protein variants in Cattle

Researches conducted on indigenous cows (Zebu type), buffaloes and exotic cows (*Taurine* type) have revealed

that A1 allele is more frequent in exotic cattle (A1 milk) while Indian native dairy cows and buffaloes have only A2 allele and hence are a source for safe milk i.e A2 milk (Mishra *et al.*, 2009). The A2 allele gene in Indian milk breeds of cows and buffaloes are 100% (Red Sindhi, Sahiwal, Tharparkar, Gir and Rathi), other Indian breeds

used for farming, is around 94 per cent (Joshi, 2011) and while in foreign breeds (HF and Jersey), it is around 60 per cent (NBAGR, 2011). A1 -casein is absent in the milk of pure Asian and African Cattle (Ng-Kwai-Hang and Grosclaude, 2002). So, our indigenous cows and buffaloes produce A2 milk.

1. Allelic and genotypic frequency of Beta casein gene across the Indian cattle breeds (Mishra *et al.*, 2009)

Sl. No.	Cattle breeds	Allelic Frequency		Genotype Frequency		
		A1	A2	A1A1	A1A2	A2A2
1	Sahiwal	0	1	0	0	1
2	Red Sindhi	0	1	0	0	1
3	Tharparkar	0	1	0	0	1
4	Gir	0	1	0	0	1
5	Kangayam	0	1	0	0	1
6	Nimari	0	1	0	0	1
7	Red Kandhari	0	1	0	0	1
8	Amritmahal	0	1	0	0	1
9	Malvi	0	1	0	0	1
10	Kankrej	0	1	0	0	1
11	Hariana	0	1	0	0	1
12	Rathi	0	1	0	0	1
13	Mewati	0	1	0	0	1
14	Malnad Gidda	0.096	0.904	0	0.191	0.809
15	Kherigarh	0.109	0.891	0	0.218	0.783

2. Occurance of Beta casein gene variants in various cattle breeds and countries (Kaminiski *et al.*, 2007)

Sl. No.	Cattle breeds	Countries	Frequency of Beta casein alleles			References
			B	A1	A2	
1	Jersey	Germany	0.186	0.093	0.721	Ehrmann <i>et al.</i> , 1997
		Denmark	0.350	0.070	0.580-360	Bech <i>et al.</i> , 1990
		New Zealand	-	0.123	0.591	Winkelman and Wickham, 1997
		USA	0.290-0.370	0.090-0.220	0.490-540	Enennam <i>et al.</i> , 1991
2	HF	Norway	-	0.400	0.490	Lien <i>et al.</i> , 1993
3	Guernsey	USA		0.010		Swaissgood, 1992
4.	Brown Swedish	Germany	0.170	0.108	0.705	Ehrmann <i>et al.</i> , 1997
5.	Simmental	Croatia	0.150	0.190	0.630	Curik <i>et al.</i> , 1997
6	Ayrshire	UK	0-0.003	0.006	0.004	Swaissgood, 1992

3. Allelic and genotypic frequency of Beta casein gene across the Indian Buffalo breeds (Mishra *et al.*, 2009)

Sl. No.	Buffalo breeds	Allelic Frequency		Genotype Frequency		
		A1	A2	A1A1	A1A2	A2A2
1	Murrah	0	1	0	0	1
2	Mehsana	0	1	0	0	1
3	Marathwada	0	1	0	0	1
4	South Kanara	0	1	0	0	1
5	Manipuri	0	1	0	0	1
6	Assamese Swamp	0	1	0	0	1
7	Nilli-Ravi	0	1	0	0	1
8	Pandharpuri	0	1	0	0	1

Milk protein and BCMs

Bovine milk protein is composed approximately of 80% casein and 20% whey (Shah, 2000; Niki *et al.*, 1994; Martien *et al.*, 1994). But according to some researchers whey proteins constitute about 14% (McLachlan, 2001; Roginski, 2003). It contains four components namely s1 (CSN1S1, 39–46%), s2 (CSN1S2, 8–11%), (CSN2, 25–35%), and (CSN3, 8–15%) of total caseins (Eigel *et al.*, 1984; Roginski, 2003; Rijnkels, 2002) whereas human

milk casein is composed of primarily β_1 and β_2 . β_1 -casein is the second most abundant protein and crucial for casein micelle structure. Beta-casein is 30% of the total protein content in cow's milk. The polymorphic status of bovine β -casein is confirmed, and till date 13 allelic variants have been identified (Kaminski *et al.*, 2007). Amongst these, A1 and A2 variants are reported to be the most common allelic variants of β -casein in dairy cattle (Farrell *et al.*, 2004). The polymorphic nature and its association with

milk, fat and protein yield attracted several efforts in evaluating this locus as a potential dairy trait marker (Ikonen *et al.*, 1999; Caroli *et al.*, 2004; Kucerova *et al.*, 2006). Consumption of milk of certain breeds of cow, buffaloes, sheep and goat may result in the release and possible absorption of bioactive peptides like BCMs. These peptides yielded by the digestion of β -casein have opioid effects similar to morphine, and so named β -casomorphins (β -CMs). The β -CMs have unique structural features that impart a high and physiologically significant affinity with the binding sites of endogenous opioid receptors (Meisel and FitzGerald, 2000). Of the protein variants A1 β -casein yields BCM-7 whereas A2 β -casein does not give rise to BCM-7 upon digestion (Woodford, 2006; Bell *et al.*, 2006). β -CM-7 has been well established as a potent bio-active peptide with opioid activity.

Mechanism of BCM-7 generation in the Small intestine

The A1 and A2 variants of bovine β -casein differ at amino acid position 67 with histidine in A1 and proline in A2 milk. This polymorphism leads to key conformational changes in the secondary structure of expressed β -casein protein (Elliot *et al.*, 1999; McLachlan, 2001). Due to presence of histidine at amino acid 67 position, digestion of A1 β -casein milk releases a 7 amino acid bioactive peptide called beta-casomorphin 7 (BCM-7) in small intestine, while proline in A2 milk at 67 position prevents the split at this particular site and generates peptide BCM-9 (Roginski, 2003; Kostya *et al.*, 2004). It is believed that generation of BCM-7 is the major causative factor associated with A1 milk related health disorders. However, A2 β -casein not been linked to any of such health issues (Kaminski *et al.*, 2007).

Impact of A1 and A2 milk on human health

Milk from dairy cows is providing a high quality source of protein and an essential micronutrients like energy, calcium, magnesium and phosphorus to human beings since long time (Bell *et al.*, 2006). A significant relationship was observed between bovine milk protein consumption and the incidence of type 1 diabetes and CVD (McLachlan, 2001; Laugesen and Elliott, 2003; Elliott *et al.*, 1999; Thorsdottir *et al.*, 2000, Virtanen *et al.*, 2000; Monetini *et al.*, 2002; Birgisdottir *et al.*, 2002), arteriosclerosis (Tailford *et al.*, 2003). Besides, neurological disorders such as schizophrenia and autism (Woodford, 2006), and sudden infant death syndrome were also appeared to be known to potentiated by milk (Sun *et al.*, 1999; Sun and Cade, 1999; Sun *et al.*, 2003). The relationship between disease risk and bovine milk consumption is the focus of this review with special emphasis to A1 and A2 hypothesis.

In many of the medical literature we get to know the link between the development of ischemic heart disease (CVD) and specific milk protein intake (McLachlan, 2001; Laugesen and Elliott, 2003; Tailford *et al.*, 2003). Besides, some populations such as the Masai (East African) and Samburu (Northern Keyan) had virtually no heart disease despite consuming a diet rich in animal milk. But that milk fortunately came from Zebu cattle, which is a breed that carries the A2 allele exclusively (McLachlan, 2001). Western countries, which had similarly high bovine milk consumption from predominantly the Holstein breed, jersey and other breeds had a greater incidence of CVD

than nations with low milk consumption. It is so because people of small nations consume fortunately A2 milk. But epidemiological analyses concerning the two alleles of β -casein and the incidence of CVD underscores the apparent relationship between the risk of chronic disease and milk protein variant intake (McLachlan, 2001; Laugesen and Elliott, 2003). Above all many researchers have claimed the relationship of A1 milk with many human diseases like CVD, autism, schizophrenia etc (Woodford, 2011, Mishra *et al.*, 2009).

The Food and Agriculture Organisation (FAO) (2012) has reported increase in many chronic diseases arising out of milk. These diseases if studied thoroughly can be alleviated by improving the health benefiting milk components. The β -casein composition of the protein fraction has become of special interest recently because of a possible relationship between β -casein genotype and the health of population of consumers. Genetic variants in bovine β -casein gene (A1 and B) release a bioactive peptide, β -casomorphin-7 (BCM-7) upon digestion, responsible for many human disorders like Type 1 diabetes, autism, schizophrenia and heart diseases but A2 milk does not cause such type of illnesses (Keith Woodford, 2007; Mishra *et al.*, 2009; Sodhi *et al.*, 2012). Infants may absorb β -CM-7 due to an immature gastrointestinal tract. Adults, on the other hand, appear to reap the biological activity locally on the intestinal brush boarder. β -CM-7 can potentially affect numerous opioid receptors in the nervous, endocrine, and immune systems. Whether there is a definite health benefit to milk containing the A2 genetic variant is unknown and requires further investigation unlike harmful effects of A1 milk.

With the increasing intake of dairy products, the consumption of other essential nutrients such as zinc, vitamin A, magnesium, folate, and riboflavin are also increasing (Weinberg *et al.*, 2004). However, we are able to get only about 700 mg of calcium per day, which comes primarily from dairy products (Weinberg *et al.*, 2004; Ervin *et al.*, 2004). This amount is against the recommended amount of 1,000–1,500 mg (NIH Consensus Development Conference, 1994). Most other food sources contain low concentrations of calcium. Calcium content of milk, may reduce the risk of osteoporosis and colon cancer (Heaney *et al.*, 1999; Birt *et al.*, 1999) and including milk in the diet may promote weight loss (Phelan *et al.*, 2003). The ideal calcium to magnesium ratio for the human body should be 2:1. The A1 milk's ratio is 10:1. By relying on A1 cow's milk for calcium, we will have magnesium deficiency and imbalance, but A2 milk does not cause such imbalances. Magnesium relaxes us, helps improve digestion, is anti-inflammatory in action, involved in nerve and muscle function, de-toxifier, increases alkalinity of the blood and flexibility of the tissues. Magnesium is required for the body to produce and store energy. Without magnesium there is no energy, no movement, no life. So, A1 milk will lower magnesium levels whereas A2 milk does not.

The inflammation from A1 milk casein causes lymphatic congestion and metabolic suppression. A1 milk worsens acne, eczema, upper respiratory infections, asthma and allergies. It causes digestive problems, not because of the lactose but because of massive histamine release from casomorphin. Ear infections, bronchitis, tonsillitis are

driven by A1 casein. A1 milk casein causes endometriosis because of its inflammatory and immune-disruptive effect. Endometriosis is a gynecological condition in which cells from the lining of the uterus (endometrium) appear and flourish outside the uterine cavity, most commonly on the membrane which lines the abdominal cavity. Many women with infertility may suffer from endometriosis and other reproductive complications.

CONCLUSION

We can now conclude that we should drink A2 milk only as it prevents us from milk related health complications especially from A1 milk. More research is also required to prove the reality of the hypothesis of A1 and A2 milk. In this aspect, Government's support is needed to accomplish the above anomalies of milk quality and standards to improve the health of the people.

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