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Superiority of A2 Milk Over A1 Milk: A Boon for Human Health

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Abstract

Milk is a complete food as it contains all essential micro-nutrients needed for growth and development of human health as well as for neonate animals. However, milk derivative peptides may cause deleterious effect on human health by elevating risk for type I diabetes (DM-1), coronary heart disease (CHD), schizophrenia and autism. The higher occurrences of these diseases have relationship with consumption of variants A1, B and C beta–casein from cow's milk. The production of BCM-7 is more in A1 milk than A2 milk and the difference is basically at 67th position of the beta casein chain. Due to presence of histidine at amino acid at 67th position, digestion of A1 β-casein milk releases a 7 amino acid bioactive peptide called β-casomorphin 7 (BCM-7) in small intestine, while proline in A2 milk at 67th position prevents splitting at this particular site. So propensity is now towards consumption of A2 milk. It is a matter of great concern for the health of people in India.

Introduction

Milk contains all essential micro-nutrients so it is called a complete food. It contains immunoglobulin's, hormones, growth factors, cytokines, nucleotides, peptides, polyamines, enzymes and several others bioactive peptides. The lipids in milk are emulsified in globules coated with membranes and proteins are in colloidal dispersions as micelles. The casein micelles are seen and observed as colloidal complexes of protein and salts, especially with calcium. Lactose and most other minerals are present in solution form. Cow's milk contains about 87.7% water, 4.9% lactose (milk sugar), 3.4% fat, 3.3% protein and 0.70% Minerals.

Bovine milk contains about 32g protein/liter (USDA, 2007). Bovine milk contains huge array of proteins from antimicrobials to hormones and enzymes to antibodies (Clare et al., 2000). Milk usually has two different types of proteins i.e. caseins and whey proteins. Casein is about 80% (Niki et al., 1994) and rest is whey protein. Milk caseins are assembled into proteins and minerals macromolecules and thereby form casein micelles. The structure of the micelles shows k-CN primarily on to the surface and protects the micelle structure from destabilization. Casein shows phosphorylation as they are basically phoshoproteins. Casein molecular mass is about 18–25 k Da. These are quite heterogenous in nature as it develops through post-

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translational modifications and alternative splicing of the gene product and genetic polymorphisms (Caroli et al., 2009). Milk proteins (e.g. secretory immunoglobulin A, lactoferrin, 1-antitrypsin, β-casein and lactalbumin) in human digestive tract appear as peptides or whole proteins and their functions depending upon their relative resistance towards digestive enzymes. Biological function of caseins is to carry calcium and phosphate and to form a clot in the stomach for efficient digestion. Milk usually has three different types of casein protein i.e. Alpha, Beta and Kappa casein. Whey protein is of two types i.e. alpha-lactalbumins and beta-lactglobulins. Casein contains four components namely αs1 (CSN1S1, 39–46%), αs2 (CSN1S2, 8–11%), β (CSN2, 25–35%) and κ (CSN3, 8–15%) of total caseins (Eigel et al., 1976; Rijnkels, 2002).

A1 and A2 Milk

Amongst the milk constituents, beta casein has gained importance and popularity amongst the health conscious people due to its recent health related issues. The β-CN constitutes about 30% of total CN in bovine milk and is encoded by the CSN2 gene on chromosome 6 (Rijnkels, 2002). This gene is highly polymorphic and 12 different genetic variants of β-CN based on gene polymorphisms and protein sequences have been identified. Alpha-Casein have 9 variants and Beta-Casein have 12 variants (A1, A2, A3, B, C, D, E, F, G, H1, H2, I) but A1 and A2 variants are reported to be the most common allelic variants of β-casein in dairy cattle (Farrell et al., 2004). Kappa-casein has 11 variants. 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. So A2 milk is the milk that contains only the A2 type of beta-casein protein whereas A1 milk contains only A1 beta casein type variant. A1 protein variant is commonly found in milk from crossbred and European breeds of cattle. Foreign breeds like HF and Jersey contains around 60% of A1 protein (Priyadarshini et al., 2018). Indigenous cow (Zebu type), buffalo and exotic cows (taurine type) have shown that A1 allele is frequent in exotic cattle while Indian native dairy cow and buffalo have only A2 allele (Mishra et al., 2009). The Milk of Indian breeds of cows (Red Sindhi, Sahiwal, Tharparkar, Gir and Rathi) and buffaloes have 100% A2 allele gene. A1 β-casein is absent in the milk of pure Asian and African Cattle So, our indigenous cows and buffaloes produce only A2 milk.

Chemistry of A2 into A1 beta-casein

A2 is recognised as being the original or ancestor beta-casein gene in modern cattle. Scientists believe the difference originated as a mutation that occurred between 5000 and 10,000 years ago—as cattle were being taken north into Europe—when the proline at position 67 was replaced by histidine, with the mutation subsequently spreading widely throughout herds in the Western world through breeding. Originally all domesticated cows produced milk containing only A2 type of beta-casein. Natural mutation resulting into variant of the A2 protein appeared in a proportion of cows of European breeds producing a casein variant called A1 beta-casein.

Beta casein is a chain of 209 amino acids in length. Cows which produce this protein in their milk with a proline at 67th position are called A2 cows and 67th Position's change from proline to histidine created A1 beta-casein (Greenberg et al,. 1984, Roginski, 2003). A bioactive peptide with seven-amino-acid called β-casomorphin-7 (BCM-7), is released by digestion of A1 β-casein with pepsin, leucine amino peptidase and elastase in the small intestine. But milk with A2 β-casein, which has alternative proline at 67th position, prevents a split at this site. Proline has a strong bond to BCM 7, which does not release from the milk in the gut, so that essentially no BCM 7 is found in the urine, blood or GI tract of indigenous A2 cows. On the other hand, histidine, the mutated protein, only weakly holds on to BCM 7, so it is liberated in the GI tract of animals and humans who drink A1 cow's milk. One amino acid difference allows the formation of beta-casomorphin-7 (BCM7) via digestion. The effects on human health of this tiny protein fragment called beta-casomorphin-7 (BCM7) which is a powerful opioid or narcotic as well as being antioxidant. BCM-7 is an exorphin having potential to elicit opioid activity via its affinity to both mu- and delta receptors on a range of tissues and organs including the digestive tract, respiratory and immune systems.

These peptides yielded by the digestion of β-casein have opioid effects similar to morphine, and so named β-casomorphins (β-CMs). Due to presence of histidine at amino acid 67th 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). A1-derived BCM-7 has been shown to have a longer half-life (Panksepp et al., 1984). BCM-7 may cross the breast parenchyma–blood barrier into plasma and subsequently penetrate the blood–brain barrier to reach the central nervous system of the developing foetus (Nyberg et al., 1989). 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). A1, B and C β-casein have a histidine residue at position 67 that allows an enzymatic cleavage to occur during digestion, releasing the seven amino acid peptide, β- casomorphin 7 (De Noni and Cattaneo, 2010).

Health problems with A1 milk

Due to ingestion of A1 Milk, Increased incidences of various diseases like Type 1diabetes, Heart diseases, Autism and schizophrenia, Atherosc-lerosisand Sudden infant death syndrome (SIDS). BCM-7 has been linked as a peptide with the ability to catalyse the oxidation of LDL (Low Density Lipoprotein) in a non cation dependent fashion (Torreilles and Guerin, 1995) and this Oxidised LDL uptake by endothelium-bound macrophages leads to pathogenesis of atherosclerosis (Siow et al., 1999). BCM7 causes human health hazards as it can potentially affect numerous opioid receptors in the nervous, endocrine and immune system. Autism and schizophrenia have associated with consumption of beta casein A1 milk (Laugesen and Elliott, 2003; Tailford et al., 2003).

Elliott (1992) stated that Mice on diets having A1 β-casein got diabetic but no diabetes occurred in the mice fed with A2 β –casein. Apnoea in infants due to the consumption of bovine milk, of A1 origin, which lead to sudden death in new born (Sun et al., 2003). Protein from some cow's milk (not all the cows) raise risk for type I diabetes (DM-1) and coronary heart disease (CHD), schizophrenia and autism as Well. β-casein A1 proteins may develop and assist in the development of diabetes and cardiac diseases (Birgisdottir, 2002).A correlation between BCM-7 levels with delayed psychomotor function in formula fed human infants has been reported. Recent clinical trials report BCM-7 production to physiologically relevant levels in the gut of healthy adult humans (Boutrou et al., 2013). Neurological problems get potentiated due to the consumption of A1 milk which is being related directly to autistic spectral disorder (ASD) and schizophrenia. BCM-7 and related compounds may be involved in the etiology of a range of chronic diseases, including Type 1 diabetes, ischaemic heart disease, autism and schizophrenia (Elliott et al., 1999; McLachlan, 2001).

Bioactive peptide BCM-7 is an exceptionally powerful opioid and Serum BCM-7 has also been linked to the compromise of breathing in infants fed A1 containing formula. A behavioural study of 70 patients with childhood autism who were put on a gluten free, casein free (GFCF) diet concluded that GFCF diet had helped in reducing autism disorder symptoms (Cade et al., 2000). BCM-7 acts on lymphocytes in the intestinal wall and in some way promotes an auto-immune reaction to insulin-producing β-cells resulting in their damage and so the required amount of insulin cannot then be secreted (Elliott et al., 1997). Cieslinnska et al. (2007) experimentally shown that the level of BCM-7 in β-casein A1 hydrolysed milk was four times higher than in A2 milk. BCM-7 has been reported to bind to μ-opioid receptors located on the epithelial cells in the gut and inhibit gastrointestinal (GI) functions, which may lead to decreased GI motility and delayed transit time (Barnett et al., 2014).

Conclusion

Milk for human health ought to be drunk. But, determination of milk quality and standards to A1 and A2 milk is also required. Currently, A2 milk is being marketed as a healthier choice than regular milk. The A1/A2 debate is still up in the air. A few studies indicate that A1 beta-casein may have adverse effects in certain individuals and it is believed that generation of BCM-7 is the major causative factor associated with A1 milk related health disorders. However, the evidence is still too weak for any strong conclusions to be made. That being said, if you feel like you can tolerate A2 milk better than A1 milk, then you should definitely stick to it.

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