

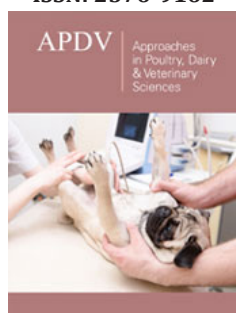
# A1 Beta Casein: Devil in the Milk- A Short Communication

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ISSN: 2576-9162



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**Submission:**  September 09, 2019

**Published:**  October 23, 2019

Volume 7 - Issue 1

**How to cite this article:** Amanuel Bekuma, Ulfina Galmessa. A1 Beta Casein: Devil in the Milk- A Short Communication. *Appro Poultr Dairy & Vet Sci* 7(1). APDV.000651.2019.  
DOI: [10.31031/APDV.2019.07.000651](https://doi.org/10.31031/APDV.2019.07.000651)

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## Abstract

Milk is the highly evolved secretion of mammary glands of mammals and the most perfect food for infants. However, casein free diet is recommended for infants with immunological sensitivities. Several variants of  $\beta$ -casein (~30% of cows' milk-proteins) are genetically determined; A1, A2, A3, B, C etc. Among the genetic variants of beta-casein, the problematic type of casein protein found in milk is the A1 beta casein, devil in the milk. A1 and A2 milk variants differ by a single amino acid, resulting in differential secondary structure and enzymatic hydrolysis, i.e. A1 but not A2  $\beta$ -casein liberates the  $\beta$ -casomorphin-7 (BCM7), which acts ~morphine. BCM7 is implicated in digestive, immune and brain development changes and strong correlation between consumption of BCM7 containing A1 milk. It is incidences of type-1 diabetes mellitus, autoimmune and cardiovascular diseases and other illness such as autism and schizophrenia are also reported. Thus, it's the nation's and government's responsibility to cease cross breeding programmes and protect purity of older (indigenous) breeds through using semen for bulls that have been tested as being A2A2 and culling of A1A1 and A1A2 cows by selective retention of A2A2 calves.

**Keywords:** A1 and A2 Beta Casein; Beta Casomorphin; Devil in the milk

## Introduction

Milk is the highly evolved secretion of mammary glands of mammals and the most perfect food for infants. With a balance of protein, carbohydrate and fat coupled with essential minerals, dairy milk has been a staple food to many populations, especially for early infant development where milk and/or milk-based formulas are the only source of nutrition [1]. Milk has about 86% water, 4.6% lactose sugar, 3.7% triglycerides, 2.8% milk protein, 0.54% minerals and 3.36% other constituents [2]. Milk protein constitutes of 36%  $\alpha$ -Casein, 27%  $\beta$ -Casein, 9%  $\kappa$ -casein and 27% peptides and amino acids. The protein fraction composition of  $\beta$ -casein has become of special interest recently because of a possible relationship between  $\beta$ -casein genotype and the health of consumers. Milk that contains A1  $\beta$ -Casein and A2  $\beta$ -Casein are known as A1 milk and A2 milk, respectively [3,4]. 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.

## A1 and A2 $\beta$ casein and their differences

Casein represents about 80% of total protein in cows' milk, about 30- 35% of which is  $\beta$ -casein [5]. Within  $\beta$ -casein, there are a number of variants which are genetically determined. A1, A2 and B are the most common variants. A1 and, to a lesser extent, B have been implicated in the literature in relation to human disease. A1 and B  $\beta$ -casein have a histidine at position 67 that allows an enzymatic cleavage to occur releasing a 7 amino acid called ' $\beta$  casomorphin 7' ( $\beta$ CM-7) [6,7]. The A2 variant has a proline at position 67 so that  $\beta$ CM-7 is not released. This difference is explained in the following amino acid structure.

The variant A1 is the dominant  $\beta$ -casein in milk from the black and white Holsteins and Friesians cows while A2  $\beta$ -casein is dominant in milk from the yellow and red Jerseys and Gurnseys cows. Accordingly, the A1  $\beta$ -casein milk is dominant in Europe (excluding France), USA, New Zealand, and Australia. Currently, New Zealand is working to shift cow milk  $\beta$ -casein from A1 to A2. The A2 variant is the sole or dominant  $\beta$ -casein in milks from other animal

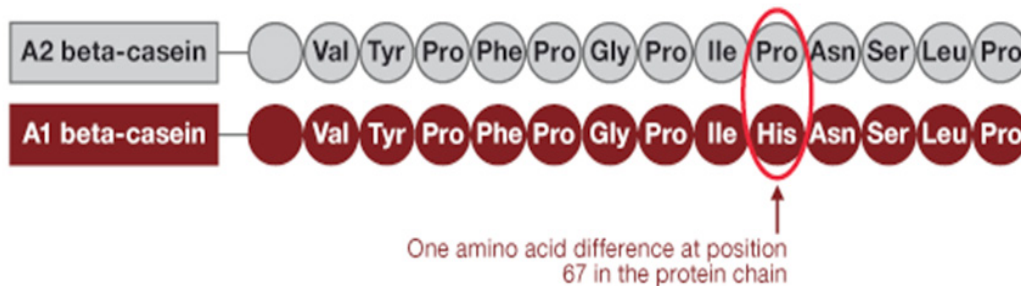
species such as buffalo, camels, goats, and sheep [8,9] and a recent human intervention study has shown a significant negative association of A1  $\beta$ -casein on gut function [10-12].

**A1 Beta Casein: Devil in the Milk**

A2 beta-casein is found in all Western, African and Indian cattle and buffalo. A1 beta casein is carried only by the cows of European breeds, all of which belong to the sub-species *Bos Taurus*. Beta-casein allele frequency in indigenous cattle (*Bos Indicus*) and

buffalo breeds reported to have 99 to 100% presence of the A2/A2 genotype and A1/A1 genotype is absent among them. So, almost all the indigenous cow and buffalo breeds are homozygous for the A2 beta-casein allele. The picture is different among European breeds. The Holstein carries the A1 and A2 beta-casein alleles almost in equal distribution. Jersey has an A2 allele frequency somewhat higher than this. But some Jersey cows carry one "B" beta-casein allele which can release of BCM-7 far more [11] (Figure 1).

**Protein chain showing amino acids in A1 and A2 beta-casein**

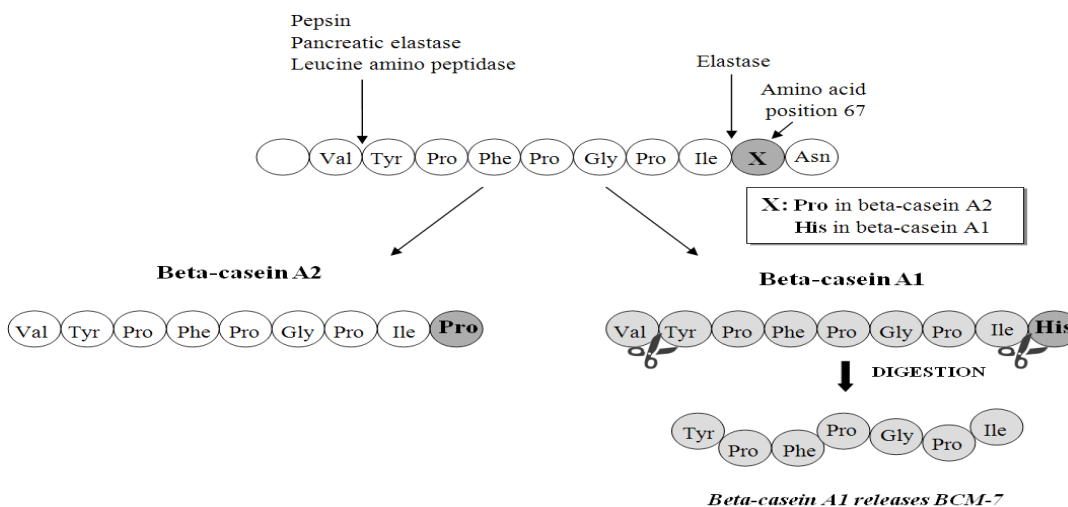


**Figure 1:** Structure of A1 and A2 Beta Casein variants.

Among the genetic variants of beta-casein: A1, A2, A3, B, C, D, E, F, G, H1, H2, and I, the problematic type of casein protein found in milk is the A1 beta casein, devil in the milk [8-13]. It's known to be the result of a genetic mutation in cattle that's believed to have occurred about 8,000 years ago in Europe. Because of the weak bonding of histidine, A1 beta casein is commonly broken down into a peptide of 7 amino acids called beta casomorphin -7 (BCM-7) during digestion. Although it's also possible for BCM-7 to be produced from A2 beta casein, it's much less likely, and if it were to happen, it would be in much smaller amounts [14].

A1  $\beta$ -casein contains a histidine residue at 67 positions, which allows cleavage of the preceding seven amino acid residues, generating the peptide  $\beta$ -casomorphin-7 (BCM-7). Only A1

beta-casein, and its siblings, beta-casein B and C, can result in betacasomorphin- 7 (BCM7) production and A2 and A3 beta-casein do not produce BCM7 during digestion. BCM-7 is a digestion product of beta casein, can be absorbed through the gut wall in people with leaky gut syndrome, and is a possible irritant chemical to those with autism and other neurological diseases [14]. BCM7 is problematic because it's an oxidant that's particularly known for damaging low density lipoproteins (LDL). Many of the problems relating to BCM7 can only occur if it's absorbed through the stomach or intestines into the bloodstream. However, BCM7 is too large to be absorbed through a healthy intestinal lining. BCM-7 can cross the gastrointestinal wall to enter the systemic circulation and influence systemic and cellular activities via opioid receptors and affects: GI motility, GI absorption, and GI secretion, GI immune function [13].



**Figure 2:**

The difference between the A1 and A2 beta caseins of just a single amino acid sounds like a minor difference, but is quite significant because the bond between histidine and its adjacent amino acid in A1 beta casein is much weaker and much more easily broken than the bonding of proline in A2 beta casein, which is responsible for negative effect on human health. The A1 beta-casein protein derived BCM-7 can affect many opioid receptors in the endocrine, nervous and immune system. Infants are having more chance of absorption of BCM-7 through their comparatively immature gastro-intestinal tract than the adults who are having a chance of showing local reaction in the intestine. In short, the hypothesis that a high intake of milk containing A1  $\beta$ -casein promotes conditions as heterogeneous as Risk of Type 1 diabetes, heart Disease, Sudden Infant Death Syndrome (SIDS) and other illness like neurological disorders, such as autism and schizophrenia is intriguing and potentially important. Therefore due to its negative consequence on human health, A1 Beta Casein is devil in the milk Figure 2.

### Conclusions and Perspectives

Since, the A2 milk (older cow's milk) should only be recommended as it prevents the human beings from milk related health complications, which are due to A1 milk (Exotic cattle's milk), in our opinion, the warranted actions at present by the relevant government agencies involve:

- I. Increasing the frequency of alleles coding for Pro-67 by selective breeding;
- II. Breeding for A2A2 cows is based on using semen for bulls that have been tested as being A2A2;
- III. the breeding process can be speeded up by selective culling of A1A1 and A1A2 cows and by selective retention of A2A2 calves;
- IV. Funding further research, especially clinical research; and in this aspect, government's support is needed to accomplish the above anomalies of milk quality and to conserve the indigenous breed's purity.

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