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Casein Variants and Challenges in the Valorization of Camel Milk as a Healthy Alternative to Cow Milk

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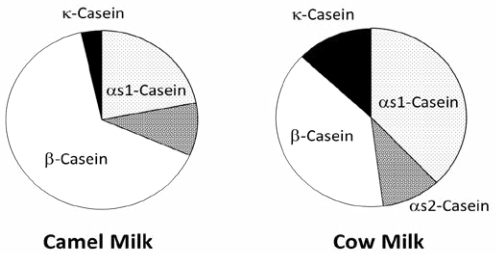
In 1997, Elliott et al. [1] published a paper showing that feeding of non-obese diabetic (NOD) mice with cow milk A1 β-casein, and not with A2 β-casein, leads to the development of diabetes mellitus type-1 (DM-1). Soon after, Elliot et al. [2] published another paper presented an epidemiological evidence of a strong correlation (R^2 =0.982, p<0.01) between the daily consumption of A1 β-casein from cow milk (*Bos Taurus*) and the incidence of DM-1 in children (0-14 y) in 19 developed countries. In contrast to children consuming milk from dairy cows of north European origin (e.g. Friesian, Ayrshire, British Shorthorn, and Holstein), DM-1 was found to be rare in the Masai children with high consumption of milk from Zebu cows (*Bos indicus*). Both cows' milk β-caseins contain 209 amino acids that differ only in the amino acid at position 67, this being histidine in the A1 and proline in the A2 milk variants. *In vitro* digestion studies with pepsin, leucine aminopeptidase, and elastase have shown that breakdown of the A1 β-casein in the small intestine releases β-casomorphin-7 (BCM-7, Tyr^{60}-Pro-Phe-Pro-Gly-Pro-Ile-His^{67}), a bioactive seven-amino-acid opioid-like peptide. It was shown that the presence of proline at position 67 of the A2 variant prevents the breakdown of the protein at this site. Based on this difference, Elliot et al. [1] suggested that the etiology of DM-1 by A1 β-casein and not by A2 β-casein may be related to the release of the peptide BCM-7, which has strong immunosuppressant activity. The collected evidence from the epidemiological, biochemical, pharmacological, immunological, and animal and human studies was reviewed [3,4].

The variant A1 is the dominant β-casein in milk from the black and white Holsteins and Friesians cows while A2 β-casein is dominant in milk from the yellow and red Jerseys and Gurnseys cows. Accordingly, the A1 β-casein milk is dominant in Europe (excluding France), USA, New Zealand, and Australia. Currently, New Zealand is working to shift cow milk β-casein from A1 to A2. The A2 variant is the sole or dominant β-casein in milks from other animal species such as buffalo, camels, goats, and sheep. In addition to the above-mentioned effect of A1 β-casein, two recent animal studies have shown negative effects of this protein variant on digestive transit time and gut inflammation [5,6] and a recent human intervention study has also shown a significant negative association of A1 β-casein on gut function [7]. Moreover, consumption of bovine A1 β-casein was also associated with allergy, neurological disorders such as autism, schizophrenia, and sudden death in children [3].

Unlike cow milk, camel milk is repeatedly reported to have *inter alias* antidiabetic [8,9] and anti-hypertensive effects. This milk is rich in insulin and insulin like proteins, lyzozymes, lactoferrin, and lactoperoxidase. The antidiabetic effect of camel milk was demonstrated in clinical intervention as well as in epidemiological studies. An epidemiological study in India revealed that populations who regularly consume camel milk have zero incidence of DM-1 as compared to 5.5% in other communities that do not consume this milk [9]. It was also shown that daily consumption of about 500 mL of camel milk by DM-1 patients led to 30-35% reduction of their insulin requirements with significant decrease in blood glucose levels [8].

Similar to other mammals, the caseins are the main component of camel milk. There are four main types of milk caseins, i.e. αs1-casein, αs2-casein, β-casein, and κ-casein. Table 1 shows that the relative distribution of these four caseins in camel milk is clearly different from that of cow milk, especially for the β-casein and κ-casein [10,11]. The low prevalence of κ-casein in camel milk is believed to contribute to the instability of ultra-high temperature (UHT) treated milk [12] as well as to cause difficulties in curding during cheese making [13].

According to the accepted hypothesis [14], UHT treatment of cow milk denatures the whey β-lactoglobulin leading to its unfolding and activation of its sulfhydryl groups to form complexes and/or disulfide bonds with κ-casein in the outside of the casein micelles. This interaction between β-lactoglobulin and κ-casein weakens the interaction between the κ-casein and the other proteins in the casein micelle leading to the release of the cross-linked βκ-complexes from the casein micelles. The freed βκ-complexes may then form linkages with other proteins and when they attain certain critical concentration, they eventually create a three-dimensional gel matrix that lead to a semi-rigid gel structure. The chemistry of the denatured β-lactoglobulin and the nature of its interaction with κ-casein are unknown and may involve oxidation reactions and/or Maillard reactions (with lactose). It is not known why camel milk is more susceptible to post-UHT age-gelation compared to cow milk but camel milk caseins are known to be more hydrophobic than those of cow milk. It was also speculated that the



αs1-Casein	207 amino acids (Type A)	199 amino acids (Type B)
αs2-Casein	178 amino acids	207 amino acids (Type A)
β-Casein	217 amino acids (Type A2)	209 amino acids (Type A1)
κ-Casein	162 amino acids	169 amino acids

Data from Kappeler et al. 1998 and Al Haj and Al Kanhal 2010

Table 1: Relative distribution of the main caseins in cow and camel milk.

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technological difficulties facing the processing camel milk compared with cow milk are probably more due to the different proportions of the individual caseins than to the structural differences between these proteins [10]. Moreover, the extra instability of camel milk compared to cow milk may be due to its content of α-lactoglobulin rather than the β-lactoglobulin present in cow milk The lack of knowledge of the the chemistry of gelation after ultra-high temperature treatment of camel milk presents a great challenge for camel milk processing industries.

Making cheese from camel milk presents another difficulty and only soft unripe cheese can be obtained. Rennet enzymes used in cheese initiate the coagulation of milk by cleaving the κ-casein at the Phe_{105}–Met_{106} bond releasing its negatively charged C-terminus. This exposes the hydrophobic core of the casein micelles leading to aggregation, gel formation and phase separation of the milk into curd and whey [15]. In addition, chymosine also cleaves α- and β-caseins where cleavage at the bond Phe_{23}–Phe_{24} in α_{S1}-casein leads to softening of the cheese and another cleavage at the Leu_{192}–Tyr_{193} imparts bitterness to the cheese. The production of an acceptable soft ripe cheese from camel milk has recently been improved by the production of a transgenic camel chymosin Hansen© (Denmark). Fermentation-produced camel chymosin (FPCC) circumvents the problem of bitter peptides by the unique high specificity towards camel κ-casein, thus providing a way to produce high-quality camel cheese. Improved technologies are still needed to develop new cheese types that would achieve international acceptance. However, it was recently discovered that chymosin from camel was actually better at initiating coagulation in cow's milk. Once the mechanism of casein coagulation is understood, it may be possible to develop even better ingredients for the dairy industry.

Set yoghurt has not been achieved with camel milk but several traditional fermented products have been made by fermentation of camel milk with *Streptococcus thermophilus*, *Lactobacillus delbrueckii* subsp. *bulgaricus*, and *Saccharomyces* yeast. Examples of these products include Airag and Orom (Mangolia), Chal (Turkey and Iran), Garis (Sudan), Kefir (USSR), Oggtt (Saudi Arabia), Shubat (Kazakhstan), Susa, Suusacc and Karuur (Somalia and East Africa). Different fermentation strategies are used in the production of these liquid products with different tastes and flavors. Unlike the case with other ruminant milks, camel milk does not coagulate well during fermentation to produce a firm gel-like structure possibly due to the presence of anti-microbial agents such as lactoferrin, lysozyme, and lactoperoxidase that inhibit the growth of the starter cultures used in the manufacture of yoghurt.

In addition to these technical difficulties, there is a serious gap in the understanding of camel milk proteins chemistry, which is very important when planning to develop new foods or food ingredients from camel milk. Therefore, intensive research is needed in the chemistry of camel milk proteins, and their associated properties to develop innovative and functional products and ingredients from camel, including yoghurts, cheeses, powders, and long-shelf life milk.

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