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A 100-Year Review: Progress on the chemistry of milk and its components[1]

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ABSTRACT

Understanding the chemistry of milk and its components is critical to the production of consistent, high-quality dairy products as well as the development of new dairy ingredients. Over the past 100 yr we have gone from believing that milk has only 3 protein fractions to identifying all the major and minor types of milk proteins as well as discovering that they have genetic variants. The structure and physical properties of most of the milk proteins have been extensively studied. The structure of the casein micelle has been the subject of many studies, and the initial views on submicelles have given way to the current model of the micelle as being assembled as a result of the concerted action of several types of interactions (including hydrophobic and the formation of calcium phosphate nanoclusters). The benefits of this improved knowledge of the type and nature of casein interactions include better control of the cheesemaking process, more functional milk powders, development of new products such as cream liqueurs, and expanded food applications. Increasing knowledge of proteins and minerals was paralleled by developments in the analysis of milk fat and its synthesis together with greater knowledge of its packaging in the milk fat globule membrane. Advances in analytical techniques have been essential to the isolation and characterization of milk components. Milk testing has progressed from gross compositional analyses of the fat and total solids content to the rapid analysis of milk for a wide range of components for various purposes, such as diagnostic issues related to animal health. Up to the 1950s, research on dairy chemistry was mostly focused on topics such as protein fractionation, heat stability, acid–base buffering, freezing point, and the nature of the calcium phosphate present in milk. Between the 1950s and 1970s, there was a major focus on identifying all the main protein types, their sequences, variants, association behavior, and other physical properties. During the 1970s and 1980s, one of the major emphases in dairy research was on protein functionality and fractionation processes. The negative cloud over dairy fat has lifted recently due to multiple reviews and meta-analyses showing no association with chronic issues such as cardiovascular disease, but changing consumer misconceptions will take time. More recently, there has been a great deal of interest in the biological and nutritional components in milk and how these materials were uniquely designed by the cow to achieve this type of purpose.

Key words: milk protein, functionality, dairy chemistry

INTRODUCTION

Several critical reviews have been published in the *Journal of Dairy Science* on the progress of milk chemistry and its components. Jenness (1956) reviewed the previous 50 yr of progress in the *Journal of Dairy Science* edition commemorating the 50th anniversary of the formation of ADSA, and Harper (1981) and Brunner (1981) updated key achievements and milestones for the 75th anniversary edition. Many of the key historical references can be found in these reviews, and only selected references are highlighted in this review. Jenness (1956) stated, "Much of the progress made in the last half-century in the basic knowledge of the chemistry of milk has consisted of filling in details in a picture whose broad outlines were already delineated." In the past 50 yr, dairy chemistry has moved on from the previous emphasis on organic chemistry to studies related to biochemistry, physical chemistry, nutrition, processing-induced reactions, physiology, genetics, genomics, and structural biology.

Another key factor in progressing our knowledge in the milk composition field was the creation of the ADSA Committee on Milk Protein Nomenclature, Classification, and Methodology, which published its first report in 1956 (Jenness et al., 1956) in the *Journal of Dairy Science*. That report recognized a total of 8 milk proteins, whereas in the 2004 report (6th ed.; Farrell et al., 2004), 13 major milk proteins were identified along with their many genetic variants. The report also clarified that some of the CN have different levels of phosphorylation and were not in fact new types of pro-

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teins. This committee recognized that older empirically named protein fractions were often in fact mixtures, and to avoid confusion they published their preferred nomenclature for these new individual components. In subsequent decades this committee continued to publish updated reports, which also appeared in the *Journal of Dairy Science*. The work of this committee helped standardize the naming of various milk protein fractions and variants, correcting errors and incorporating primary structures as sequencing data became available. There are likely hundreds of proteins present in milk at concentrations as low as microgram per liter levels, and many of these proteins are likely associated with minor components, such as the lipoprotein membranes.

Looking back over the past 100 yr (see Appendix Table A1), we can note that by 1917 (when the *Journal of Dairy Science* was first published) considerable information was already available on the gross chemical composition of milk as well as seasonal or breed variation. We refer to *Dairy Chemistry* by Richmond (1914) to benchmark what was known about dairy chemistry around 100 yr ago. Many minor components have since been discovered and characterized, including many vitamins, enzymes, and trace elements. Over the past 50 yr numerous studies have been conducted on the effect of feed and lactation on the detailed composition of milk as well as the effect on functional properties such as rennet coagulation. In 1917, milk proteins were considered to consist of only 3 main fractions: CN, lactalbumin, and lactoglobulin. Over the next 40 yr a major focus was on the fractionation of milk proteins by a range of experimental methods and new analytical approaches.

Over the past 30 yr there has been growing awareness of the incredible diversity of nutrients in milk as well as how these milk components provide various types of important bioactivities well beyond just providing nutrition. This focus on the nutritional diversity of milk has been assisted by developments such as improved analytical techniques that facilitated lower detection levels, the exploitation of a range of –omic techniques, use of a wide range of in vitro and in vivo models, and greater knowledge of the composition of human milk as well as the milks of other breeds.

In 1917, knowledge on how milk components were synthesized within the mammary gland was limited. It is now well established that most major milk constituents are synthesized in the mammary gland from components obtained from the blood. However, considerable modification occurs in the mammary gland, including creation of the finished structure (e.g., CN micelle, triglycerides, lactose; Bauman et al., 2006). In his review for the *Journal of Dairy Science* issue commemorating the 75th anniversary of the ADSA, Brunner (1981) warned young scientists reviewing the thousands of scientific papers published in dairy chemistry about being lured into complacency thinking everything worth knowing has been investigated. He stated, "Nothing could be further from the truth!" He argued that we did not fully understand the milk protein system and its organization, the complexities of milk synthesis at the cellular level, or the purpose of many components. Although much has been learned since that review, we still do not fully understand the very complex biological structures present in milk.

A CENTURY OF PROGRESS IN DAIRY CHEMISTRY

Advances in Analytical Techniques

Progress in identifying milk components and describing their detailed physical and chemical properties is linked to the development of new analytical techniques. Many advances in analytical equipment have been made over the past 100 yr, including analytical centrifugation, electrophoresis, thin-layer chromatography, GC, AA sequencing, electron microscopy, dynamic light scattering, neutron and X-ray scattering, rheology, MS, genomic approaches, and so on. For example, as electron microscopy developed in the 1940s it quickly showed that CN particles are large and mostly spherical (Nitschmann, 1949). Later, with improvements in electron microscopy, researchers reported that the surface was not entirely smooth, which contributed to the belief that micelles were made up of subunits. Recently, topographical electron microscopy techniques have given a 3-dimensional picture of the inside of the CN micelle, showing large voids mostly occupied by water.

The development of analytical centrifugation helped Waugh and colleagues in their classic studies of CN association (Waugh, 1971). It is notable that dairy scientists have routinely collaborated with other basic scientists to explore new physical techniques as they were being developed. For example, the first reliable measurements of the size distribution of CN micelles used dynamic light scattering. Many dairy scientists have heard about Pieter Walstra's famous experiment in which he demonstrated that rennet action reduced the average micelle size and thus provided experimental evidence for the presence of κ-CN hairs on the micelle surface (Walstra et al., 1981). This development came about because Victor Bloomfield was already using dynamic light scattering to measure micelle size, and Walstra came along one afternoon to talk to him while he was on sabbatical at the University of Minnesota. A few years later David Horne, again using dynamic light scattering, demonstrated the collapse of the hairy