Milk Protein and Their Uses (The Future of Milk Protein)

Professor John Lucey
Director of the Wisconsin Center for Dairy Research
University of Wisconsin-Madison

Center for Dairy Research *"Solution Based Research Backed by Experience, Passion and Tradition"*

1

Outline

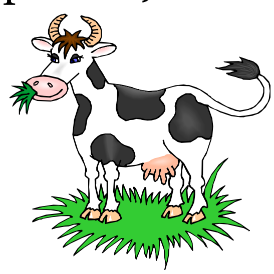
- Introduction to types of milk protein
- Introduction to milk protein ingredients (powders, and modified powders)
- Uses/applications of milk proteins
- Key growth areas for use of milk proteins
  - Functionality in many food applications
  - Excellent nutritional quality
- Some comments on A2 milk
  - What is it and what's the evidence
- Conclusions

2

2

Types of Milk Proteins

- Caseins are those proteins that precipitate at pH 4.6 (~ 80% of total protein)
- Whey (or serum) proteins are those proteins that remain soluble (~ 20% of total protein)



3

3

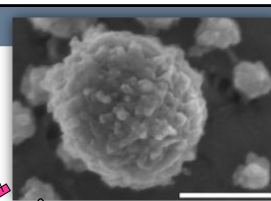
Types of Caseins

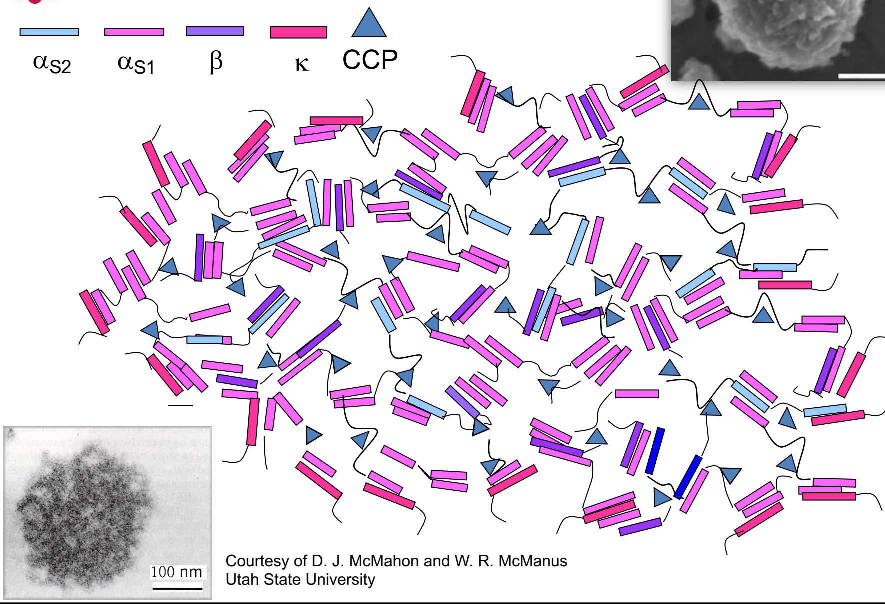
α_s-caseins (50%)	β-casein (35%)	κ-casein (13%)
• Very rich in phosphate (for calcium binding) • Not present in human milk • Precipitates with acid (yogurt)	• Rich in phosphate (for calcium binding) • Two main genetic variants (A1 and A2) • No solid evidence that A2 genetic variant is "healthier"	• Stabilizes the micelle structure • Hydrolyzed by rennet enzyme to start the cheesemaking process

4

4

Casein Micelle





Courtesy of D. J. McMahon and W. R. McManus
Utah State University

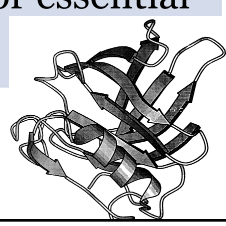
5

5

Types of Whey Proteins

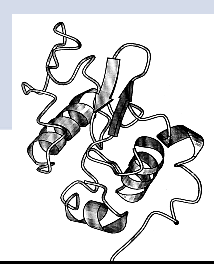
β-lactoglobulin (50%)

- Excellent nutritional properties (rich in branched AA)
- Not present in human milk
- No clear or essential function



α-lactalbumin (20%)

- Required for lactose synthesis
- Thus, present in every milk type



6

6

Comparison of Whey Proteins and Caseins

Caseins
1. Random coil (high proline content, already denatured)
2. Marginal sulfur (essential) amino acid content
3. Normal level of branched chain amino acids
4. Phosphorylated (for Ca binding)
5. Colloidal suspension (casein micelles)
5. Slow digestion, forms a clot
6. Soluble at neutral pH but insoluble close to pH 4.6
7. Stable to heat (even to retort)
8. Uneven distribution of hydrophobic & hydrophilic amino acids
9. Non-crystalline (non-globular protein)

Whey proteins
1. Ordered secondary/tertiary structures (low proline content)
2. Good source of essential AA (High in sulfur AA)
3. High content of branched chain amino acids (for muscles)
4. Not phosphorylated
5. Small soluble proteins (e.g. 2-3 nm)
5. Rapid digestion in small intestine
6. Soluble over large pH range when they are native
7. Readily denatured by heat
8. Even distribution of hydrophobic & hydrophilic amino acids
9. Crystalline structures reported

7

7

Proteins in Human and Cows' Milk

Protein	Human Colostrum	Human Milk, Normal	Cows' Milk
Casein	5[a]	2.5[a]	26
α-Lactalbumin	3	2	1.2
β-Lactoglobulin	0.0	0.0	3.2
Serum albumin	0.4	0.3	0.4
Immunoglobulins	2.5	0.8	0.7
Lactoferrin	3.5	1.5	<0.1
Lysozyme	0.5	0.5	10^{-4}

Note: Approximate averages in grams per kg; incomplete.

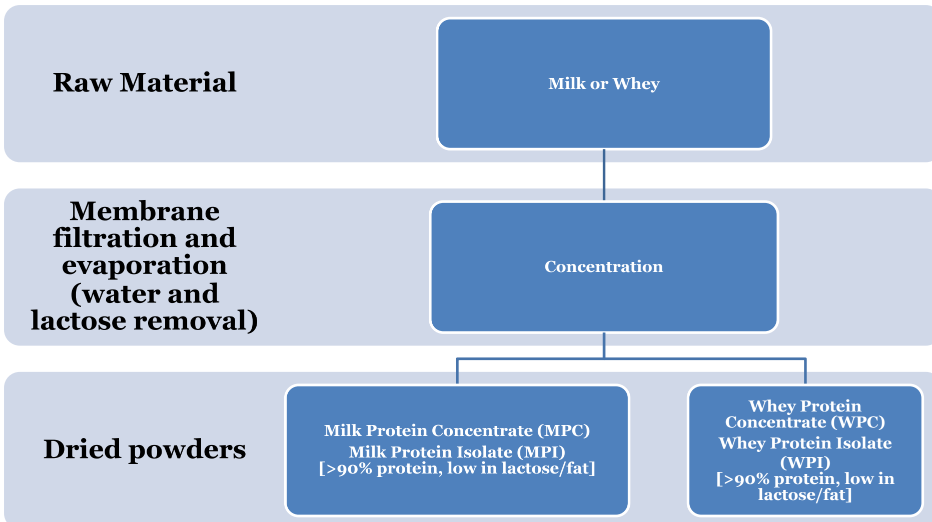
[a] Predominantly β- and κ-casein.

Walstra et al. 2006. Dairy Science and Technology

8

8

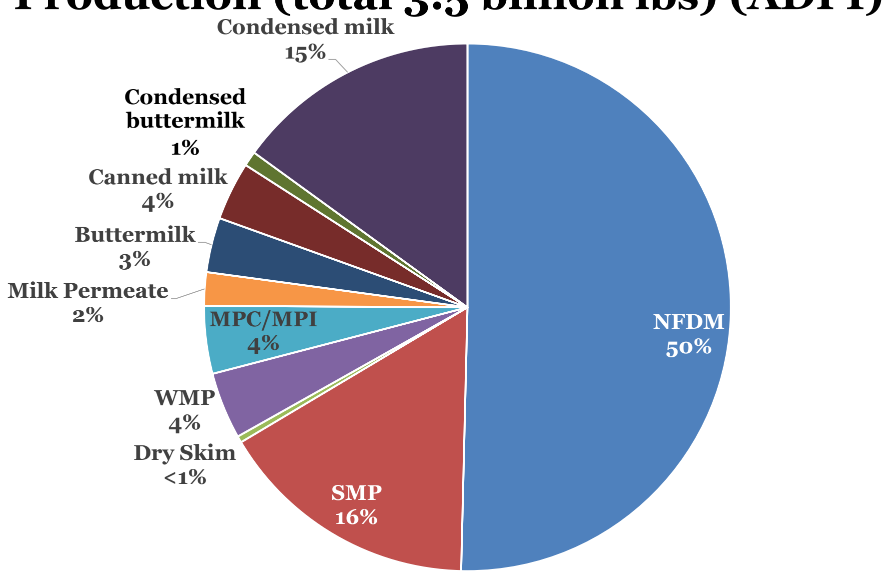
Milk Protein Ingredients



9

9

2018 Milk-based Dairy Ingredient Production (total 3.5 billion lbs) (ADPI)



10

10

What's Driving Current (and also likely Future) Popularity of Dairy Proteins?

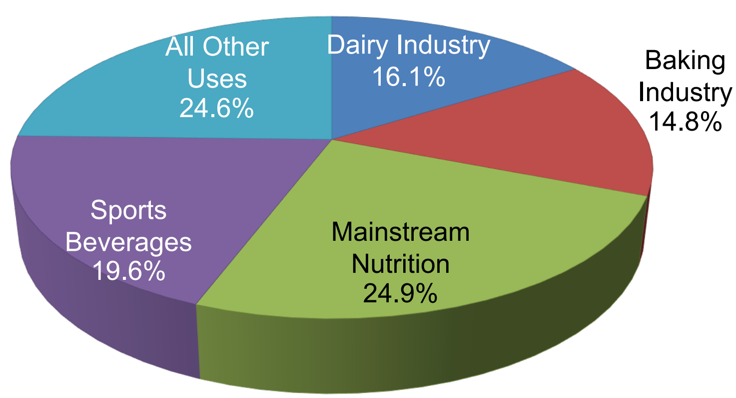
1. Versatility in many food applications
2. Excellent quality of dairy protein (superior)

11

11

Milk Protein Concentrate Utilization

(Production in 2018 was 145 M pounds)



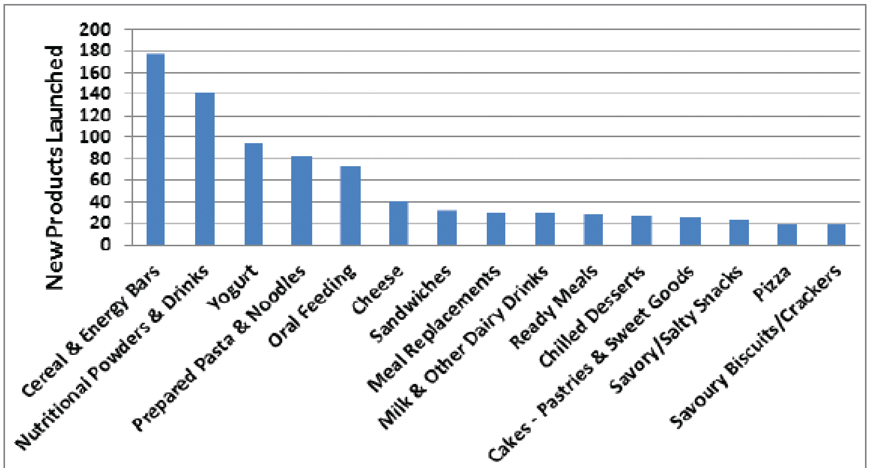
ADPI, 2019

12

12

High Protein Ingredients Used in Many Food Products

Figure 5: Number of products launched containing MPC as an ingredient (top 15 major sectors).

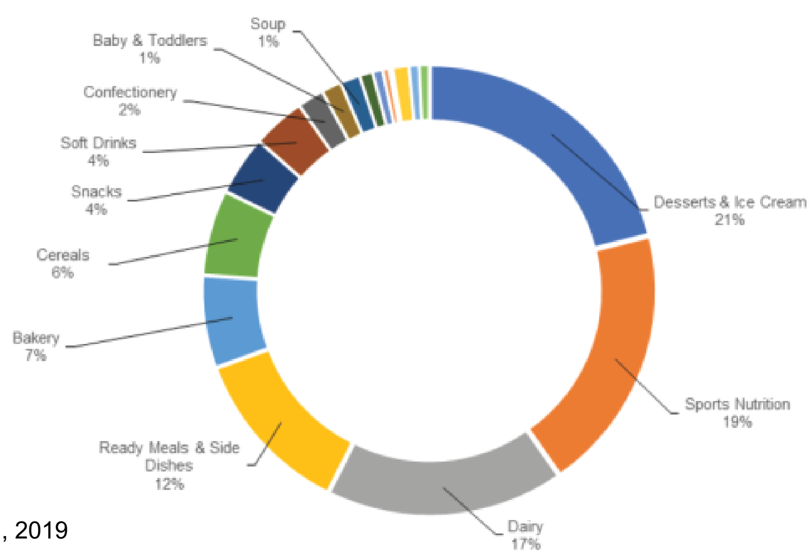


13

www.usdairy.com/~/media/usd/public/mpc_tech_report_final.pdf

13

Product Introduction using MPC per Category (2018) USA

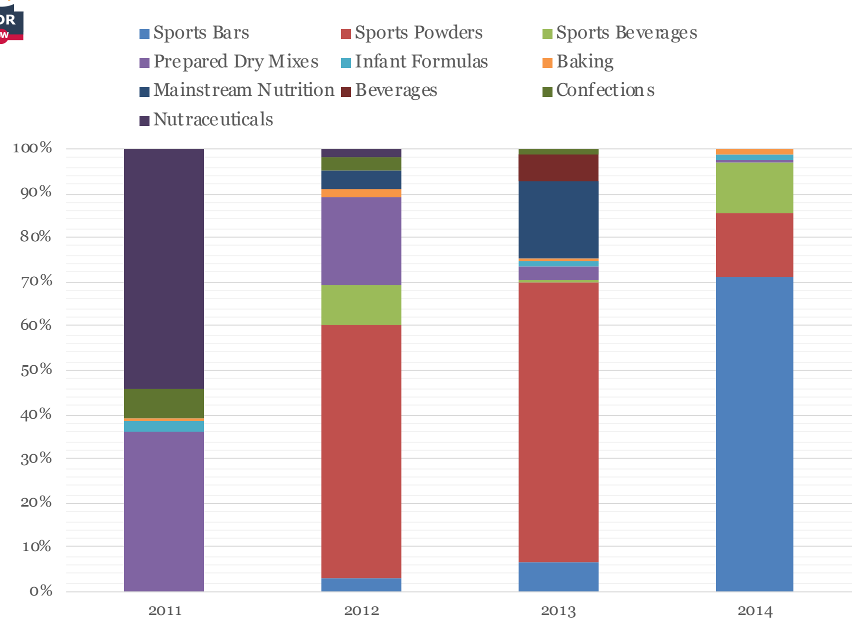


ADPI, 2019

14

14

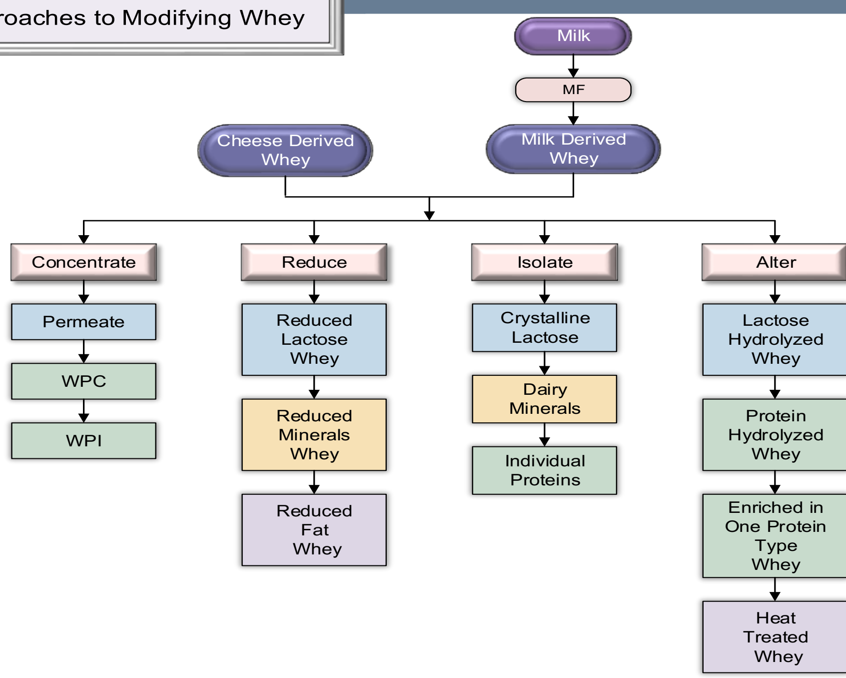
Whey Protein Isolate Utilization



15

15

Approaches to Modifying Whey



16

16

Whey Application Opportunities

Whey Type	Possible Applications
High protein WPC/WPI	Sports/nutrition drinks, dry mixes, protein bars
Reduced fat WPC	Clear protein drinks, protein gels for sports
Hydrolyzed whey protein	Heat stabile protein drinks, softer protein bars
Reduced mineral whey	Infant formula, improved heat stability
Heat treated whey	Enhanced water binding for sauces, processed meats
Enriched in one type of protein, e.g., alpha-lactalbumin	Infant formula

17

17

Concentration of Key Amino Acids in Dairy

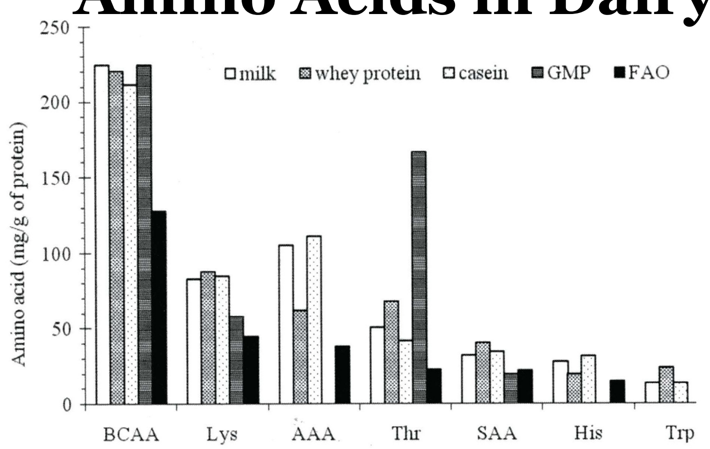


Fig. 16.3 Distribution of indispensible amino acids (IAAs) in milk, milk protein fractions and glycomacropeptide (GMP) in comparison to human requirements recommended by the FAO/WHO/UNU (2007) (*Source*: FAO/WHO/UNU, 2007; Boutrif, 1991; USDEC, 2011; Etzel, 2004)

Pellegrino et al. (2013) Nutritional quality of milk proteins in Advanced Dairy Chemistry, 4th Edn

18

18

Content of Leucine and Branched Chain Amino Acids

Table 16.4 Content of leucine and branched-chain amino acids (BCAA) (leucine, isoleucine and valine) in milk and other food sources

Protein	Leucine (g/100 g protein)	BCAA
Whey isolate	14	26
Milk	10	21
Egg	8.5	20
Soy isolate	8	18
Navy beans	7.6	16
Whole wheat flour	7	15

Sources: Layman and Baum (2004) (source: USDA Food composition tables) and Young and Pellet (1990)

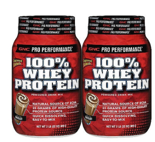
Pellegrino et al. (2013) Nutritional quality of milk proteins in Advanced Dairy Chemistry, 4th Edn

19

19

Key Benefits of Dairy Proteins

- Very rich in branched chain amino acids (e.g., leucine)
  - Helps initiate protein synthesis
  - Important for muscle recovery
  - Helps with weight loss (helps maintain blood glucose level)
  - Synergies with exercise
  - Can promote healthy aging (sarcopenia)
- Protein intake also promotes satiety (feeling full)



McGregor & Poppitt (2012) Nutrition and Metabolism 10:46 Cooper et al. (2016) Int. J. Dairy Tech. 69:13

20

20

High Protein Diets

- Suggestions of getting 25-30 grams of protein per meal (in order to get enough leucine, whey protein is very rich in leucine)

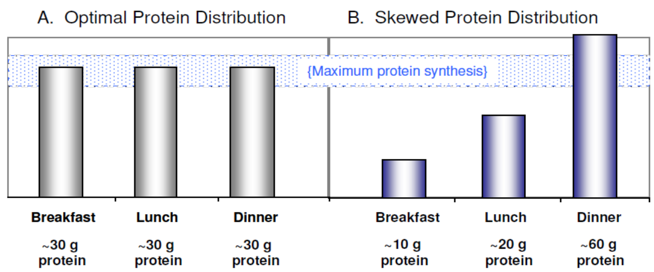


Figure 1
Protein distribution at meals. A) Ingestion of 90 grams of protein, distributed evenly at 3 meals. B) Ingestion of 90 grams of proteins unevenly distributed throughout the day. Stimulating muscle protein synthesis to a maximal extent during the meals shown in Figure 1A is more likely to provide a greater 24 hour protein anabolic response than the unequal protein distribution in Figure 1B. (Adapted from Paddon-Jones & Rassmussen Curr Opin Clin Nutr Metab Care 2009, 12: 86–90.)

Layman (2009) Nutrition and Metabolism 6:12

21

21

Products Using Milk Protein Concentrate

Macaroni and Cheese

Abbott-PediaSure
7g protein

Sugar Free Chocolate

22

22

Products Using Milk Protein Isolate

Lactose sensitive Infant Formula

Abbott-EAS Protein Bar
15 g protein

Cookies'N Cream Nutritional Shake – Cytosport-21 g protein

Thin crust pizza with 27 g protein

23

23

Weight Management Drinks

Dairy protein for satiety and weight management

10 g protein

6 g protein

20 g protein

5 g protein

24

24

Muscle Recovery Drinks

Whey protein for muscle protein synthesis

12 g protein

16 g protein

20g protein

12 g protein

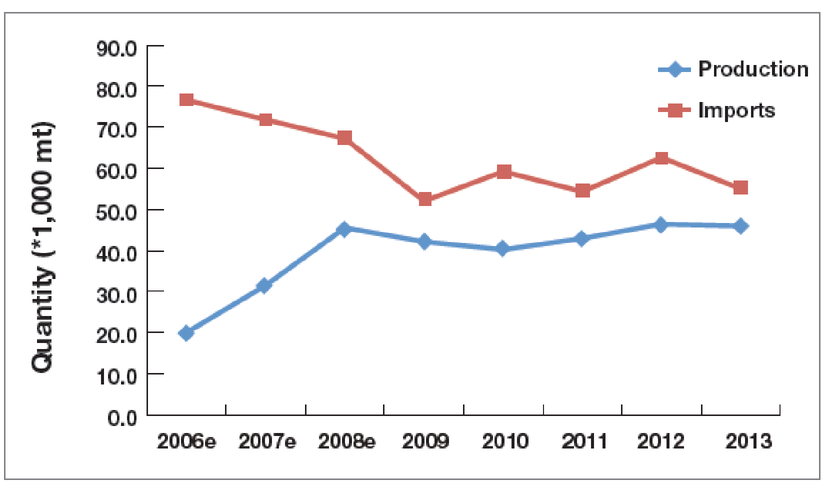
20g protein

25

25

Increased Domestic Production of High Protein Milk Products

Figure 4: Production and import of MPC in USA (2006-2013, in 1,000 mt).



26

Source: U.S. Dairy Export Council

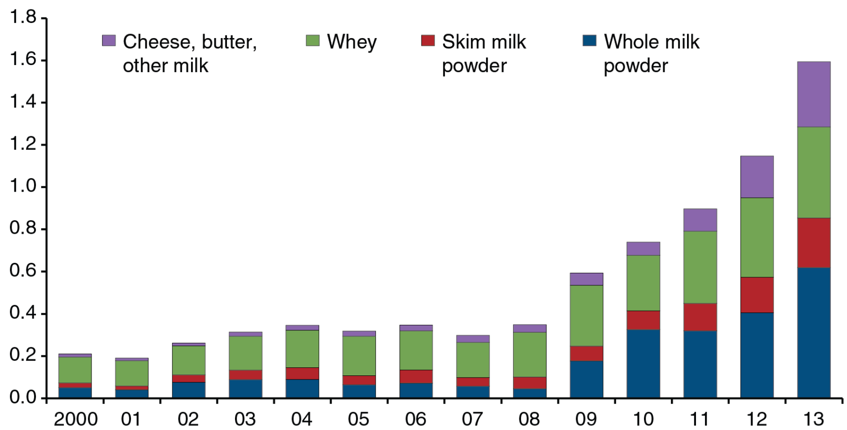
www.usdairy.com/~/media/usd/public/mpc_tech_report_final.pdf

26

Growing Export Opportunities for Dairy Protein Products (e.g., China)

China's dairy imports, 2000-13

Million metric tons



Source: USDA, Economic Research Service analysis of China's customs statistics reported by the Global Trade Atlas (2014).

27

27

Conclusions about Future of Milk Proteins

- Growth in higher protein powders (less lactose)
- Diverse uses of milk proteins in many food products
- Many techniques to modify or improve protein functionality
- Increased focus on nutritional products (protein bars, weight management, beverages, infant foods, foods for seniors, supplements)
- Interest in individual proteins and their isolation (e.g., lactoferrin, which can cost >$1000 per kg depending on purity)
- Increasing export opportunities (dairy exports worth >$6 billion in 2019)

28

28

What is A2 Milk?

What is the scientific evidence?

29

29

Milk Protein Polymorphism

- All of the main milk proteins have genetic variants
- Genetic variants are minor amino acid differences in the same protein (can be just 1 amino change)
- These variants occur at different frequencies within breeds (i.e., some are rare, others are common)

30

30

Beta-casein A1 vs. A2

- Amino acid polymorphism in β-casein
  - One amino acid difference (out of 209 amino acids)
- β-casein makes up ~30% of cow milk protein
- Most breeds produce a mixture of A1 and A2 β-casein
- 8,000 years ago a natural single-gene mutation occurred in Holsteins (A1)

31

31

TABLE 3.2
Gene frequencies of the polymorphs of the major milk proteins for common breeds[c]

Polymorph	*Holstein-Friesian*			*Guernsey*		*Jersey*			*Ayrshire*			*Brown Swiss*	
β-Caseins													
Location	US^a	US^b	UK^b	US^a	US^b	US^a	US^b	UK^b	US^a	US^b	UK^b	US^a	US^b
Number tested	526	632	85	262	196	298	37	47	202	45	29	235	23
Gene frequency													
A^1	0.49	0.31	0.66	0.06	0.01	0.09	0.22	0.09	0.67	0.72	0.60	0.15	0.14
A^2	0.49	0.62	0.24	0.88	0.98	0.54	0.49	0.63	0.32	0.28	0.40	0.72	0.66
A^3	0.01	0.05	0.04	0	0	0	0	0	0.01	0	0	0	0
A	0.99	0.98	0.94	0.94	0.99	0.63	0.71	0.72	1.00	1.00	1.00	0.87	0.80
B	0.01	0.02	0.06	0.01	0.01	0.37	0.29	0.28	0	0	0.10	0.18	
C	0	0.001	0	0.05	<0.01	0.003	0	0	0	0	0	0.03	0.02
D	0	0	0	0	0	0	0	0	0	0	0	0	0

Most breeds produce a mixture of A1 and A2 β-casein
US Holsteins are a mixture with substantial amounts of A1 in most herds
Guernsey almost all A2.
Jersey and Brown Swiss have low A1.

Advanced Dairy Chemistry – 1 Proteins, Fox & McSweeney
3rd ed. (2003) Kluwer Academic/Plenum Publishers

32

32

Beta-casomorphin-7 (BCM-7)

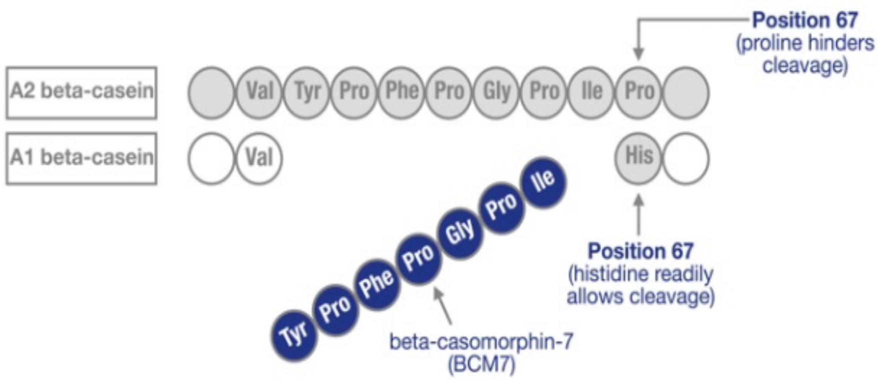


Figure 1: Release of beta-casomorphin-7 [reference: adapted from Woodford K, (2007)].

Tyr^{60}-Pro^{61}-Phe^{62}-Pro^{63}-Gly^{64}-Pro^{65}-Ile^{66}

Digestion enzymes can potentially create this fragment or peptide

33

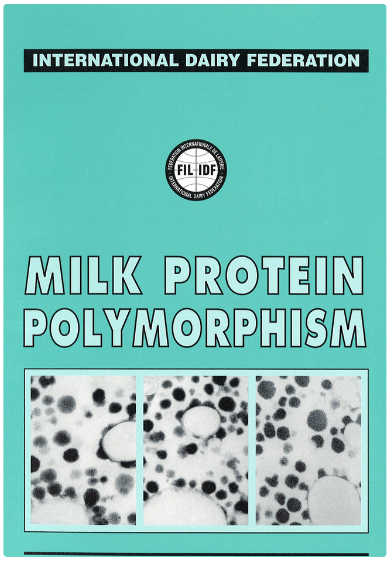
33

BCM-7

- Exogenous opioid peptide
- Potential to elicit opioid activity on a range of tissues and organs via its affinity to mu- and delta-opiate receptors
  - Responses to pain and stress
- "Bioactive peptides" are physiologically active in our body, e.g., anti-hypertensive peptides

34

34

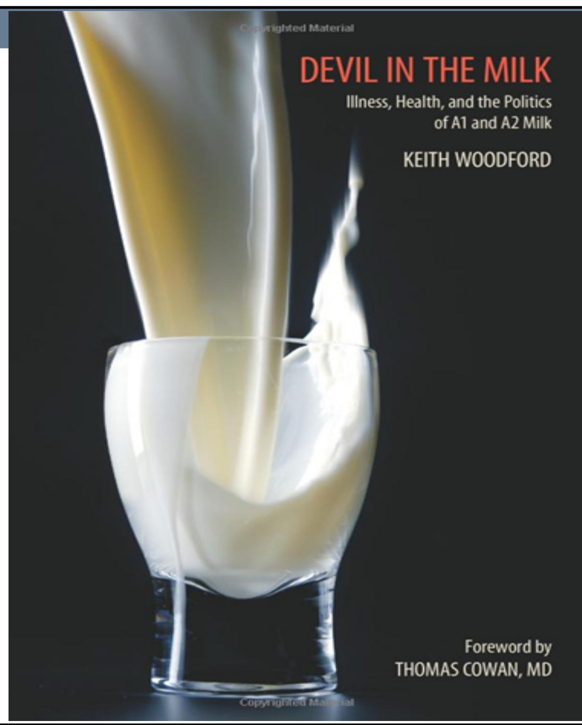


IDF Conference (1997) Palmerson North, New Zealand was where Prof. Elliot first proposes his **hypothesis** that A1 milk was implicated in risk of serious diseases

- Type 1 diabetes mellitis (DM-1)
- Coronary heart disease
- Autism
- Schizophrenia

35

35



36

36

A2 Milk Company (a2MC) Literature

- This milk does not contain the A1 milk protein which some link to serious illnesses.
- Highlights Prof Woodford's book showing countries with a high intake of A1 milk also have a high incidence of type 1 diabetes and heart disease.

Woodford K, (2007). Devil in the Milk: Illness, Health and Politics: A1 and A2 Milk. Wellington New Zealand: Craig Potton Publishing.

37

37

European Journal of Clinical Nutrition (2005) 59, 623–631
© 2005 Nature Publishing Group All rights reserved 0954-3007/05 $30.00
www.nature.com/ejcn

REVIEW

The A2 milk case: a critical review

AS Truswell[1]*

[1]*Human Nutrition Unit, University of Sydney, Sydney, Australia*

This review outlines a hypothesis that A1 one of the common variants of β-casein, a major protein in cows milk could facilitate the immunological processes that lead to type I diabetes (DM-I). It was subsequently suggested that A1 β-casein may also be a risk factor for coronary heart disease (CHD), based on between-country correlations of CHD mortality with estimated national consumption of A1 β-casein in a selected number of developed countries. A company, A2 Corporation was set up in New Zealand in the late 1990s to test cows and market milk in several countries with only the A2 variant of β-casein, which appeared not to have the disadvantages of A1 β-casein.

The second part of this review is a critique of the A1/A2 hypothesis. For both DM-I and CHD, the between-country correlation method is shown to be unreliable and negated by recalculation with more countries and by prospective studies in individuals. The animal experiments with diabetes-prone rodents that supported the hypothesis about diabetes were not confirmed by larger, better standardised multicentre experiments. The single animal experiment supporting an A1 β-casein and CHD link was small, short, in an unsuitable animal model and had other design weaknesses.

The A1/A2 milk hypothesis was ingenious. If the scientific evidence had worked out it would have required huge adjustments in the world's dairy industries. This review concludes, however, that there is no convincing or even probable evidence that the A1 β-casein of cow milk has any adverse effect in humans.

This review has been independent of examination of evidence related to A1 and A2 milk by the Australian and New Zealand food standard and food safety authorities, which have not published the evidence they have examined and the analysis of it. They stated in 2003 that no relationship has been established between A1 or A2 milk and diabetes, CHD or other diseases.

European Journal of Clinical Nutrition (2005) **59**, 623–631. doi:10.1038/sj.ejcn.1602104

38

38

Does A1 milk increase risk for any disease?

- European Food Safety Authority report: no evidence for a cause-effect relationship between A1 milk and any disease (De Noni, FitzGerald et al. 2009).

From - David Dallas, Ph.D. Assistant Professor, School of Biological and Population Health Sciences Nutrition, Oregon State University 39

39

efsa European Food Safety Authority

EFSA Scientific Report (2009) 231, 1-107

SCIENTIFIC COOPERATION AND ASSISTANCE

SCIENTIFIC REPORT OF EFSA

Review of the potential health impact of β-casomorphins and related peptides [1]

Report of the DATEX Working Group on β-casomorphins

(Question N° EFSA-Q-2008-379)

Based on the present review of available scientific literature, a cause-effect relationship between the oral intake of BCM7 or related peptides and aetiology or course of any suggested non-communicable diseases cannot be established. Consequently, a formal EFSA risk assessment of food-derived peptides is not recommended.

40

40

National Dairy Council's Chief Science Officer Greg Miller

NDC: 'The scientific theory behind A2 milk is interesting but it's still just that – a theory'

National Dairy Council chief science officer Dr Greg Miller argued that the evidence was preliminary, however: "*The scientific theory behind A2 milk is interesting but it's still just that – a theory,*" he **told FoodNavigator-USA in August**.

"We feel there needs to be more science conducted because we don't yet see sufficient support for the claims being made that A2 milk has unique benefits. A2 is another choice in the dairy case and it's good for consumers to have options. But, the view of National Dairy Council is that A2 and regular milk provide similar health benefits and have equal nutrition."

https://www.foodnavigator-usa.com/Article/2018/10/23/NAD-refers-a2-Milk-ads-to-FTC-after-NMPF-challenges-easier-on-digestion-claims

41

41

Thank You

Wisconsin Center for Dairy Research

Funded by Dairy Farmers through the
Wisconsin Milk Marketing Board,
Dairy Management, Inc.,
and the U.S. Dairy Industry

Center for Dairy Research *"Solution Based Research Backed by Experience, Passion and Tradition"*

42