



Review

Whey-ing up the options – Yesterday, today and tomorrow



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ABSTRACT

Whey, first generated more than 5000 years ago, was valued in the 17th through early 19th centuries, notably as a medicinal agent against some common maladies. However, for much of history, whey has been considered a waste by-product of cheese, casein and yoghurt manufacture. Nowadays, the intrinsic value of whey components, notably the proteins, has been recognised, and a large and growing body of scientific evidence now supports the many physico-chemical, nutritional and biological properties of whey components. This evidence has established a foundation for their value as food and related ingredients. Manufacturing technologies have been, and continue to be, developed for processing whey and for isolating functional whey components in a cost-effective manner. A diverse and expanding range of whey ingredients, foods, and related products has resulted. This paper traces the history and science of whey, highlighting the quirks, struggles, accomplishments, and emerging opportunities and challenges in the field.

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1. Introduction and background

Whey was first generated serendipitously more than 5000 years ago, and since that time man's involvement with this by-product of cheese, casein and yoghurt manufacture reveals a chequered history – it has been a love-hate relationship! In the 17th, 18th and early 19th centuries whey was valued as a fashionable drink, as a medicinal agent effective against various maladies (e.g., wounds, gut ailments), and as an alternative to water for bathing.

In the 20th century, man's drinking (and bathing) habits changed, and together with a rapid expansion of dairy product manufacture, volumes of whey increased and it became a menacing by-product of the dairy processing industry. A typical proximate analysis of sweet cheese whey (e.g., from the manufacture of Cheddar cheese) and acid whey (e.g., from manufacture of casein or Greek-style yoghurt) is shown in Table 1. Notably, sweet whey contains ~50% of the total solids found in milk, including most of the lactose, and ~20% of the milk protein. For much of the 20th century, the industry has sought out the cheapest disposal method for whey, which has usually involved discharge into waterways, the ocean, municipal sewage treatment works, and/or onto fields. While these disposal methods were tolerated for a time, the very high Biological Oxygen Demand (BOD > 35,000 ppm) and Chemical Oxygen Demand (COD > 60,000 ppm) of whey, primarily due to the high content of lactose but also the protein (Table 1), prompted the introduction of strict environmental regulations in many jurisdictions that nowadays prevent disposal of untreated whey (Mawson, 1994).

In parallel with the restrictions on disposal of whey, the intrinsic value of whey components, notably the proteins, was increasingly being recognised (Kinsella & Whitehead, 1989). A large and growing body of scientific evidence now supports the many physical, chemical, nutritional and biological properties of whey proteins and other components, and this evidence has established a scientific foundation for their value as food and related ingredients. In parallel with this expanding scientific knowledge, the marketplace was becoming more sophisticated and receptive to the usefulness of whey proteins and other components, but cost-effective and industrially feasible technologies were needed for their manufacture.

Table 1

Component and related analysis of bovine sweet and acid whey, and comparison with bovine milk.^a

Component or measure	Sweet whey	Acid whey ^b	Milk
Total solids (%)	6.3	6.6	12.8
Total protein (%)	0.75	0.75	3.5
Casein	<0.05	<0.05	2.8
Whey protein ^c	0.7	0.7	0.7
Fat (%)	0.1	0.1	3.7
Ash (%)	0.5	0.8	0.7
Lactose (%)	4.9	4.9	4.9
pH	>5.6	<5.1 ^d	6.5–6.8
BOD ^e (mg O ₂ L ⁻¹)	>30,000	>35,000	140,000
COD ^f (mg O ₂ L ⁻¹)	>60,000	~80,000	218,000
Energy (kJ L ⁻¹)	~1100	~1100	~1710

^a Consolidated from data presented in Kosikowski (1979); Mawson (1994); Smithers (2008); Smithers et al. (1996); Zadov (1994), and references therein.

^b Typical composition of acid casein whey. The total solids in acid whey from Greek-style yoghurt production is <6% and the protein content is <0.2%.

^c Whey protein comprises ~50% β -lactoglobulin, ~20% α -lactalbumin, ~20% glycomacropeptide (in renneted whey only), and ~10% minor protein/peptide components (e.g., immunoglobulins, lactoferrin, lactoperoxidase, serum albumin, lysozyme, growth factors, etc.).

^d pH often <4.5 and in acid whey from Greek-style yoghurt production can be as low as 3.5.

^e BOD, Biological Oxygen Demand.

^f COD, Chemical Oxygen Demand.

Technology developments over the past more than 60 years have resulted in increasingly sophisticated manufacturing technologies for processing whey and isolating whey proteins in a cost-effective manner, and this journey continues supported by ever expanding knowledge regarding the properties of whey components. With consumer demands for more nutritious and health-promoting foods, these technologies are currently focused on retention of the nutritional and biological qualities of the whey proteins and other components. A diverse and expanding range of functional whey and whey protein ingredients and foods, specialised formulations, bio-medical and personal care products, and components for pharmaceutical manufacture has been the result (Smithers, 2008). Our relationship with whey has come full circle, from ancient wisdom to menacing by-product to nowadays a valuable raw material, supported by a growing body of science knowledge and parallel technology developments.

Continued growth in the production of dairy products, notably cheese, has seen a concomitant increase in the volume of whey worldwide (currently >200 million tonnes per year), complemented by a recent explosion in the volume of acid whey from manufacture of strained ('Greek') yoghurt. The 'ocean of acid whey' from Greek yoghurt production, notably in the USA, represents one of the industry's greatest financial and moral challenges in the 21st century (Elliott, 2013). Others include, but are not limited to, continuing downward pressure on costs, and how to better exploit the unique features of whey proteins, peptides and other components. Science and technology will continue to provide answers including, for example, (i) clever approaches to isolation of whey proteins using charged ultrafiltration membranes (Arunkumar & Etzel, 2013; 2014); (ii) reducing the cost of cleaning through modification of equipment surfaces (Barish & Goddard, 2013); (iii) discovering and exploiting the unique properties of whey peptides to improve the performance of ingredients (Selby-Pham et al., 2013); and (iv) finding clever ways to utilise lactose (e.g., as a feed material for production of galacto-oligosaccharides) (Fischer & Kleinschmidt, 2014).

This review paper traces the history of whey and whey components (notably proteins), highlighting the opportunities, accomplishments, and emerging challenges; and the role science and technology has played in whey product development and in providing the industry with a bright future.

2. Yesterday – medicinal and menacing whey

Consumption and topical use of whey has been prescribed for various therapeutic purposes (e.g., sepsis, wound healing, and stomach disease) over thousands of years (Hoffmann, 1961). Hippocrates, the father of modern medicine, prescribed whey in 460 BC for the treatment of gastrointestinal ailments and skin conditions (Susli, 1956), although the mechanism of action was unknown at the time. In the 17th, 18th and 19th centuries, whey became a popular and fashionable 'functional drink' available in inns and other eating houses (so-called 'whey houses') (Hoffmann, 1961), somewhat akin to today's coffee shops and bistros. Samuel Pepys, the famous English diarist, frequented a 'whey house' in London in the mid-1600s, and made several diary entries to this effect in 1663 (Pepys, 2012). Similarly, Joseph Priestley notes in 1754 that while he was at Daventry Academy (1752–1755) he "went with a large company to drink whey", presumably at a 'whey house' (Rail & Thomas, 1994). Menu items at these 'whey houses' included whey borse (a type of soup), whey butter, whey cheese (still popular in northern European countries), whey porridge, and whey whig (a type of herbal tea) (Tunick, 2009). For further details on the consumption of whey, among other beverages, the reader is directed to an entertaining and engrossing account by Burnett

(2012) on the social history of drinks in Britain from the 17th century to nowadays. Bathing in sweet whey also became popular in the 19th century, notably at health spas, based on its presumed skin healing and topical health-promoting properties, and the fact that it was far more economical than bathing in milk (Trelogan, 1970).

While our forebears had ancient wisdom about the remarkable medicinal properties of whey, our drinking and bathing habits changed in the first half of the 20th century, when our love affair with whey soured. The change in these habits was also accompanied by a rapid growth in the dairy industry in the early part of the 20th century, driven by end-user demands for milk and milk products globally, resulting in an expansion in cheese and casein production, and thereby an increase in whey volumes. At this stage in history, whey became a menace and was considered nothing more than a waste stream and a nuisance that stood in the way of an even greater expansion in cheese and casein manufacture. Thus, to the processors, whey deserved nothing more than to be disposed of in the most economical manner (Smithers, 2008). In this regard, options that were used included spraying onto fields and paddocks; discharge into creeks, rivers and the ocean; treatment through municipal sewage works; and use as animal feed (e.g., pigs, cows). While these approaches all provided at least a partial solution to the whey disposal issue, they were all fraught with problems, including pollution, cost, odour, and low return. Disposal provided the cheese and casein manufacturers with a short-term “out of sight, out of mind” solution to the growing volumes of whey, but these methods were never going to provide sustainable management of whey streams. Rather, effective utilisation and value addition needed to be part of the management equation.

3. Today – functional and bioactive whey

In the second half of the 20th century, the dairy processors were ‘shocked’ into action through both legislation, and a growing body of scientific and technological knowledge about whey and whey components. In this period, several milestones aligned to turn a “low-value menace”, as whey was considered at the time, into a valuable raw material.

3.1. Environmental regulations

In terms of agricultural waste streams, whey is almost unprecedented in its polluting power (Table 1) (Mawson, 1994). In the second half of the 20th century, community action groups, environmental agencies and processors alike recognised and highlighted the environmental damage being caused by the disposal of untreated whey. Eventually, governments in various jurisdictions around the world acted and, with the exception of some developing countries, it is nowadays unlawful to dispose of untreated whey into waterways or the like (Durham & Hourigan, 2007; Kosseva, Panesar, Kaur, & Kennedy, 2009; Mawson, 1994; Siso, 1996; Smithers, 2008).

3.2. Science knowledge and technology advances

In parallel with legislative restrictions on disposal of whey, knowledge of the characteristics and properties of whey components, notably the major and minor proteins and peptides, was growing; and the techniques being used to study these components becoming more sophisticated.

3.2.1. Nutritional quality

In the latter part of the 20th and early part of the 21st centuries, the literature contained compelling evidence in support of the

exceptional nutritional quality of whey protein when compared with other common dietary protein sources. The Protein Digestibility Corrected Amino Acid Score (PDCAAS) of whey protein is 1 (highest score possible) and exceeds that of meat, wheat and nuts (Table 2). Further, whey protein exceeds the Biological Value (BV) of egg protein, the former benchmark, by ~5%, and meat and soy protein by up to 30% (Smithers, 2008) (Table 2). Whey protein is also rich in essential amino acids and represents a better source of these amino acids than egg, meat and soy protein (Smithers, 2008). Whey protein also contains a large proportion of branched chain amino acids (BCAAs), important in muscle health (Rennie, Bohe, Smith, Wackerhage, & Greenhaff, 2006) and as metabolic regulators in protein and glucose homeostasis, and lipid metabolism (i.e., weight control) (Smilowitz, Dillard, & German, 2005; Zemel, 2004) and is rich in the sulphur-containing amino acids that play critical roles in one-carbon metabolism and protein folding and function, and as precursors to the potent intracellular antioxidant glutathione (Brosnan & Brosnan, 2006; Shoveller, Stoll, Ball, & Burrin, 2005).

3.2.2. Food functionality

Together with a growing recognition of the nutritional quality of whey proteins, during the second half of the 20th century the food functional traits of these proteins and other whey components were also being identified and characterised. Over the past more than 40 years, properties such as water holding, whipping and foaming, heat-set gelation, and emulsification, inherent in whey protein products in various forms of concentration and dehydration, have been studied and reported (Dagleish, 2006; Foegeding, Davis, Doucet, & McGuffey, 2002; Harper, 1984; Kinsella & Whitehead, 1989; Mangino, 1984; Morr, 1992; Nicolai, Britten, & Schmitt, 2011; Sullivan, Khan, & Eissa, 2009). Studies have also explored the effects of heat and shear processing on these functional traits (Augustin & Udabage, 2007; De Wit, 1990; Ker & Toledo, 1992; Mangino, Kim, Dunkerley, & Zadow, 1987; Morr, 1992; Nakai & Lichan, 1985; Schmidt, Packard, & Morris, 1984), and the effects of variations in the major and minor protein constituents (Regester & Smithers, 1991), and of seasonal changes in whey composition (in regions where milk is sourced from cows that are primarily pasture fed, notably Australia and New Zealand) (Regester & Smithers, 1991; Regester, Smithers, Mangino, & Pearce, 1992).

While the various food functional traits of whey proteins were attractive to food formulators and processors alike, unreliable and inconsistent performance of whey protein products restricted their

Table 2
Biological Value (BV) and Protein Digestibility Corrected Amino Acid Score (PDCAAS) of common dietary protein sources.^a

Protein	BV ^b	PDCAAS ^c
Milk	91	1.00
Casein	77	1.00
Whey protein	104	1.00
Egg	100	1.00
Soy protein	74	1.00
Wheat gluten	64	0.25
Meat	80	0.92
Peanuts		0.52

^a Consolidated from data presented in Hoffman and Falvo (2004).

^b BV is a measure of protein quality based on the proportion of absorbed protein from a food that becomes incorporated into proteins of the consumer. BV captures how readily the amino acids from the digested protein can be used for protein synthesis in the cells of the organism. The benchmark is egg protein that is assigned a BV of 100.

^c PDCAAS is a measure of protein quality based on both the amino acid requirements of humans and their ability to digest the protein. Currently accepted by FDA and FAO/WHO as the preferred measure for determining and comparing protein quality.

widespread use when they were first made available commercially. Through a better science understanding of the physico-chemical behaviour of key whey components, responsible for and influencing functional performance, this inconsistency and unreliability has been addressed (Foegeding et al., 2002; Mangino, 1984; Mangino et al., 1987; Morr & Ha, 1993; Nakai & Li-chan, 1985; Schmidt et al., 1984), and a foundation established for commercial success (De Wit, 1998). A molecular-level understanding of the key functional whey components, their modification and interactions with other components, and external influencing factors has provided a sound foundation for new food applications for whey proteins (Foegeding et al., 2002; Golding, 2013) and for lactose (Yang & Silva, 1995). In particular, the ability of whey proteins to form microstructures and to thus be used in texturisation of low-fat products, and in the formation of micro-particulate and fat mimetic ingredients (Golding, 2013; Onwulata & Tomasula, 2004; Pearce, Dunkerley, & Wheaton, 2002), has expanded the food applications base for whey protein products beyond the traditional areas reliant upon heat-set gelation, aeration, and emulsification.

3.2.3. Mass liquid processing and drying technologies

To exploit the attractive nutritional and food functional characteristics of whey components, notably the proteins, cost-effective and industrially-feasible processing technologies were required. Thus, in parallel with a deeper science understanding of the physico-chemical characteristics of the whey components that occurred in the second half of the 20th century was the development of commercial technologies capable of efficiently processing large volumes of whey. These initial technologies were primarily aimed at capturing and concentrating the desirable whey components (e.g., protein, lactose) through elimination of water, and the removal of undesirable components (e.g., ash) through demineralisation (Kosikowski, 1979).

Demineralisation, using mixed bed cation/anion exchange chromatographic resins, was the first mass processing technology used commercially to treat whey. The demineralised whey was then dried, most typically using a spray dryer, into whey powder (Kosikowski, 1979). By controlling the extent of ion removal, whey powders with varying degrees of demineralisation could be produced. A typical 90% demineralised whey powder contains about 12% protein, 83% lactose, <1% ash, <1.5% fat, and 3% moisture.

While whey powder gained traction as a key ingredient in various formulated foods and in baby formula (in which it is still a critical constituent) (Smithers, 2008 and references therein), the market demanded whey ingredients with much higher protein contents. Membrane processing technology (notably ultrafiltration; 5–300 nm pore size) was ideally suited to the treatment of large volumes of whey, but was only a fledgling commercial technology at the time. This technology, when coupled with diafiltration, allowed for the concentration of whey protein components to >75% on a dry solids basis (Atra, Vatai, Bekassy-Molnar, & Balint, 2005; Maubois, 1980). Over the ensuing decades, equipment, membrane and operational refinements have established ultrafiltration/diafiltration coupled with spray drying as essential processing technologies in a modern dairy factory for the manufacture of valuable high-protein whey products (Morr & Ha, 1993; Schuck, 2013). Notably, advances in membrane materials and construction nowadays allow for ultrafiltration/diafiltration of whey under cool conditions (<10 °C) that favours retention of functional activity and minimises protein denaturation (Atra et al., 2005). Low-fat products have also been demanded by the market, and these have been achieved using chemical pre-treatment (Damodaran, 2011; Hwang & Damodaran, 1995; Morr & Ha, 1993) and/or microfiltration (300–10,000 nm pore size) (Hanemaaijer, 1985; Rezaei, Ashtiani, & Fouladitajar, 2011) of the whey prior to ultrafiltration/diafiltration

and drying. Typical products include whey protein concentrate (WPC)-34, WPC-75 and WPC-80/85, the latter figure referring to the protein content of the powder on a dry basis. In WPC-80, other components include fat (<5%), lactose (<6%), ash (<4%), and moisture (<5%).

Advances in membrane materials (e.g., organic, ceramic), construction (e.g., spiral wound) and the control of membrane pore size have resulted in (i) nanofiltration membranes (0.1–1 nm pore size) suitable for whey demineralisation (primarily removal of polyvalent cations) that complement the chromatographic techniques and as a pre-treatment of whey to reduce ash content prior to concentration via ultrafiltration (Atra et al., 2005; Jeantet, Rodríguez, & Garem, 2000) and (ii) reverse osmosis membranes (<0.1 nm pore size) suitable for the isolation of lactose and recovery of water following whey processing. This so-called 'cow water' that remains following removal/recovery of all the whey solids is considered potable and safe to drink (Jelen, 2003), but is currently only used in-factory for cleaning purposes.

Mass liquid processing technologies, like membrane filtration, have been important in concentrating desirable whey components and removing those that are undesirable, but equally important has been powder technology. Application and advances in spray drying (and other drying techniques) has been critical in transforming whey, whey liquid concentrate, and permeate into stable dry powders for shipment and storage (Masters, 1985; Schuck, 2013). Refinements in spray dryer design and operation have resulted in several advances for improved whey component powder characteristics and application performance. These include inclusion of a fluid bed in the dryer design to allow for final drying and cooling of the powder (Patel, Patel, & Suthar, 2009); the use of modelling to control agglomeration (Verdurmen, Van Houwelingen, Gusing, Verschuere, & Straatsma, 2006); and the use of techniques for production of instantised powders (Chen & Patel, 2008). The drying of very hygroscopic whey-derived materials (e.g., permeate/lactose from ultrafiltration of whey) has been achieved using modern spray dryers and proprietary techniques (e.g., Tixotherm™ and L-TECH™). These commercial approaches appear to rely upon a combination of bottom feed to the drying chamber, heat control and recovery to improve water removal, continuous crystallisation, and a fluid bed for final powder drying.

Science, technology and engineering have underpinned the development, application and refinement of mass liquid processing and drying technologies that have established the commercial foundation for modern whey products and ingredients like whey powder, WPC-34 and WPC-75+, and instantised and hydrolysed versions of these ingredients. More than 250,000 tonnes of high-protein WPC is manufactured globally each year (USDEC, personal communication), and the demand for such WPC is so strong that production is sometimes limited by sweet whey availability. These products serve as reliable functional and nutritious ingredients in a variety of formulated foods and beverages (De Wit, 1998; Smithers, 2008; Smithers & Augustin, 2013). In a note of caution, however, modern whey protein ingredients carry a price premium, and with increasing cost pressures on food manufacturers there is now intense competition from other ingredients (e.g., soy and wheat protein) (Day, Augustin, Batey, & Wrigley, 2006).

The widespread availability of whey-derived ingredients, notably high-protein whey concentrates (WPC-75+) and hydrolysed versions, has facilitated the development and marketing of a plethora of liquid, powdered and 'ready-to-eat' retail end-products, based around whey protein as the primary ingredient. These retail products have been marketed mainly at the time-poor consumer looking for convenience and nutrition, as well as elite and 'budding' athletes (Mollica, 2012). The marketing message has been around digestibility, metabolic efficiency and amino acid balance of the

constituent whey proteins. Marketing terms such as ‘perfect’, ‘decadent’, ‘muscle’ and ‘power’ have all been used to describe these retail products. Recent messages have included muscle health, recovery after exercise, and prevention and perhaps reversal of sarcopenia (Ha & Zemel, 2003; Hayes & Cribb, 2008; Paddon-Jones & Rasmussen, 2009).

3.2.4. Sophisticated processing and valorisation of whey

The past approximately 20 years of whey processing and product development has seen a focus on maximising the value of the constituent proteins, as well as the fats and lactose (i.e., total valorisation of whey). Efforts have been directed at (i) improvements in the characteristics and applications of existing products (e.g., WPCs with higher protein content; highly purified lactose); and (ii) development of new and novel products based on isolated components in varying degrees of purity (e.g., fractions enriched in one or other of the major whey proteins). Such isolates would be ‘free’ to express their inherent functionality in the absence of other interfering components present in a mixture (Smithers et al., 1996). Both approaches called for refinements in existing processing technologies and the introduction of new ones, in the latter case for the separation and fractionation of targeted whey components. This was a period when whey was “mined” for maximum value, relying on good science knowledge of whey and whey constituents, and sophisticated processing technologies (Huffman & Harper, 1999; Smithers, 2008).

Continuous improvements in membrane processing (microfiltration, ultrafiltration, nanofiltration), including (i) tangential flow to reduce membrane surface fouling; (ii) use of modern membrane materials (e.g., organic, ceramic) and construction (spiral-wound); and (iii) more precise control over pore size and thus molecular weight cut-off, have all led to more cost-effective membrane processing and higher quality products (Charcosset, 2006). Low-fat WPC products and high-protein isolates (WPI-90+) have been the result (Morr & Ha, 1993; Smithers, 2008); together with polar lipid isolates (Rombaut & Dewettinck, 2006).

This period of whey and whey product development also witnessed the introduction of chromatographic techniques (batch, traditional fixed bed, and continuous) to whey processing, both for production of total whey protein products and for fractionation of whey into protein isolates (De Silva, Stockmann, & Smithers, 2003; Etzel, 2004; Huffman & Harper, 1999; Woonton, Kulozik, De Silva, & Smithers, 2013). Preparative chromatography is used widely in the biotechnology and pharmaceutical industries, but has often been viewed with suspicion by the dairy industry because of cost, throughput restrictions, excessive water consumption, and perceived microbiological issues (De Silva et al., 2003). Modern approaches to continuous chromatography have addressed many of these shortcomings and as such, various incarnations of continuous chromatography are being successfully used for commercial manufacture of whey protein ingredients (e.g., WPI-90+) and fractions (De Silva et al., 2003). Moreover, specialised whey protein offerings, with tailored composition and functionality for specific end-user requirements, can be manufactured using continuous chromatography through simple modifications to operational parameters (De Silva et al., 2003; Woonton et al., 2013).

The ‘holy grail’ of whey protein product evolution and development has been the cost-effective fractionation of the major (and minor) whey proteins into isolates, with varying degrees of enrichment, for commercial applications. Modern day advances in membrane technology and preparative chromatography have brought this ‘holy grail’ within reach. For decades, the fractionation of α -lactalbumin and β -lactoglobulin has been pursued using a variety of techniques reliant upon one or more of the physico-chemical differences between the two proteins (Etzel, 2004;

Huffman & Harper, 1999; Smithers et al., 1996). Successful fractionation technologies have used (i) microfiltration and ultrafiltration, either standalone or in combination, to prepare WPC products (enriched in α -lactalbumin and/or β -lactoglobulin) (Almécija, Ibáñez, Guadix, & Guadix, 2007; Bounous, 1996; Zydney, 1998); (ii) selective precipitation of α -lactalbumin from concentrated sweet whey (leaving β -lactoglobulin in solution) under specific pH and temperature conditions (Pearce, 1988); (iii) preparative chromatography using a variety of ion exchange resins (Ayers, Elgar, Palmano, Pritchard, & Bhaskar, 2002; De Silva et al., 2003; Etzel, 2004; Heebøll-Nielsen, Justesen, & Thomas, 2004); and (iv) membrane adsorbers based on charged ultrafiltration and other membranes (Bhattacharjee, Bhattacharjee, & Datta, 2006; Goodall, Grandison, Jauregi, & Price, 2008; Pouliot, Wijers, Gauthier, & Nadeau, 1999; Rathore & Shirke, 2011; Saufi & Fee, 2011). The glycomacropeptide, that can represent a substantial proportion (~20%) of whey protein solids in renneted cheese whey, has also been isolated using a combination of chromatographic and membrane techniques (Holland, Yazdi, Titapiccolo, & Corredig, 2010; LaClair, Ney, MacLeod, & Etzel, 2009).

The availability of enriched and more highly purified fractions of the major whey proteins has led to a range of new ingredients, with associated food, formula, and clinical applications. First, β -lactoglobulin-enriched WPC has been used in a proprietary blend with hydrocolloids to produce a heat-set gel material that looks, feels and behaves remarkably like solid fat (Pearce et al., 2002). This healthy fat mimetic can successfully replace non-functional fat in a variety of processed meats (e.g., low-fat hot-dogs, deli products, hamburgers, etc.) and also in baked products (e.g., low-fat muffins). This gelled food ingredient creates healthy options for a variety of high-quality, low-fat food products, because it improves succulence and mouth-feel, can be tailored for appearance and texture, and can carry colour and flavour (Ian Barlow & Bruce Aitken, personal communication). Second, the availability of purified α -lactalbumin fractions from whey has created options for the manufacture of infant formula products that more closely resemble the composition of human milk (Heine, Klein, & Reeds, 1991). In contrast to bovine milk, human milk is rich in α -lactalbumin (about 5-fold higher content) (Fig. 1) but does not contain β -lactoglobulin (Brignon, Chtourou, & Ribadeau-Dumas, 1985; Jensen, 1995; Lien, 2003). While some modern infant formula products reflect the casein:whey protein ratio of human milk (the latter has a casein:whey protein ratio closer to 1:1 when compared with bovine milk that has a casein:whey protein ratio of ~4:1) most do not reflect the mix of whey proteins in breast milk (Fig. 1). The commercial availability of α -lactalbumin-enriched fractions allows for these products to be re-formulated (Lien, 2003) (Fig. 1). While breast milk is always the best option to nourish the newborn and developing

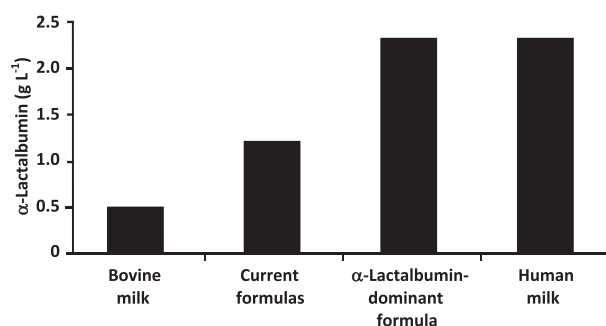


Fig. 1. Comparison of the α -lactalbumin content of bovine versus human milk, and the α -lactalbumin content of standard versus ‘alpha-enriched’ infant formula products (from Lien, 2003). Reproduced with permission of the American Society for Clinical Nutrition.

infant, for mothers who cannot breast-feed, formula products that more closely match the composition of human milk (including with other ingredients like oligosaccharides and lactoferrin) provide for better options. The Chinese infant formula market is an example of where re-formulated products, containing α -lactalbumin together with other components found at high concentration in human milk (e.g., lactoferrin, oligosaccharides), are gaining traction and commanding high prices (Williams, 2014). Finally, the glycomacropptide (~7000 Da) is unusual in that it contains no aromatic amino acids, and as such has found application in clinical foods for patients suffering from phenylketonuria (PKU) (LaClair et al., 2009; Ney et al., 2009).

While much of the focus on whey utilisation over the past 30 years has been on the proteins, lactose (the major whey solid) has also received attention, both in terms of improved isolation procedures, and applications for this carbohydrate and its derivatives (see Gaenzle, Haase, & Jelen, 2008 and Hourigan, Lifran, Vu, Listiohadi, & Sleigh, 2013 for reviews). Much of the attention has been on exploiting the physico-chemical properties of lactose in (i) designing and implementing improved isolation techniques for higher purity lactose destined for baby food and drug excipient applications (Durham, Sleigh, & Hourigan, 2004; Gaenzle et al., 2008; Hourigan et al., 2013); (ii) approaches to the effective hydrolysis of lactose into the constituent monosaccharides (Gaenzle et al., 2008; Hourigan et al., 2013); and (iii) transformation of lactose into high value derivatives, such as galacto-oligosaccharides as prebiotics (Fischer & Kleinschmidt, 2014; Splechna et al., 2006).

3.2.5. Biological and physiological activity of whey components

The ancient wisdom of our forebears in using whey for various prophylactic and therapeutic purposes has been vindicated by modern science. Whey is rich in a vast array of bioactive components including proteins, peptides, carbohydrates and lipids (Ko & Kwak, 2009; Korhonen, 2006; Korhonen & Pihlanto, 2003; Michaelidou & Steijns, 2006; Pihlanto-Leppälä, 2000; Roginski et al., 2013; Smithers, 2008; Walzem, Dillard, & German, 2002). Modern analytical and investigative tools have helped to identify and characterise these components and their derivatives, and to provide the science foundation for their applications in foods and beverages, and beyond. Over the past decade, several comprehensive reviews of dairy-derived bioactive factors have appeared in the literature and the reader is encouraged to refer to these reviews and references therein for more detail on the discovery, isolation, characterisation and application of whey bioactive components (Ko & Kwak, 2009; Korhonen, 2006; Krissansen, 2007; Roginski et al., 2013; Smithers, 2008).

Many of the whey components, most notably the proteins and peptides, have been either implicated or scientifically proven in a range of biological and physiological effects (Krissansen, 2007). These effects include (i) muscle recovery after exercise and general muscle health (Paddon-Jones & Rasmussen, 2009; Reidy et al., 2013; Tipton et al., 2004); (ii) satiety, weight management and control of obesity (Luhovyy, Akhavan, & Anderson, 2007); (iii) wound management and repair (Smithers, 2004); (iv) cardiovascular health and improvement of risk factors (Pal, Ellis, & Dhaliwal, 2010; Pins & Kennan, 2007); (v) control of microbial and viral infections (Bojsen et al., 2007; Bounous, Baruchel, Falutz, & Gold, 1993; Kussendrager & van Hooijdonk, 2000; Orsi, 2004; Regester & Belford, 1999); (vi) infant growth and nutrition (Heine et al., 1991; Lien, 2003; Lönnnerdal, 2003); and (vii) anti-cancer activity (Elías-Argote, Laubscher, & Jiménez-Flores, 2013; Gill & Cross, 2000; Krissansen, 2007; Lemonnier et al., 2003; McIntosh, Regester, Le Leu, Royle, & Smithers, 1995; 1998).

Apart from identifying the nutritional, biological and physiological characteristics of the major whey proteins (β -lactoglobulin,

α -lactalbumin and, in renneted whey, the glycomacropptide) (Chatterton et al., 2006; Ney et al., 2009; Smithers, 2008), much research and developmental attention has been focussed on the minor whey proteins and other components.

The basicity of many of the minor whey proteins (lactoferrin, lactoperoxidase, immunoglobulins, growth factors) has facilitated their simple isolation at neutral pH using cation exchange chromatographic techniques, either with traditional resins (Francis, Regester, Webb, & Ballard, 1995; Law & Reiter, 1977; Rowney, Hobman, Read, & Denichilo, 2005; Yoshida & Xiuyun, 1991) or ion exchange membranes (Chiu & Etzel, 1997). Under neutral conditions the basic proteins are readily bound to the cation exchange resin or membrane and the acidic major whey proteins easily washed away. Selective elution of the bound proteins then allows for the simple isolation of highly purified preparations of lactoferrin and lactoperoxidase, and highly enriched fractions containing growth factors and immunoglobulins. Protection of often labile bioactivity represents an important consideration in the design of any isolation procedure (Korhonen, Pihlanto-Leppälä, Rantamäki, & Tupasela, 1998). The ready availability of large quantities of enriched preparations of lactoferrin, lactoperoxidase, immunoglobulins, and growth factors has allowed for detailed studies into their various biological and physiological effects, together with associated applications.

Lactoferrin. Large quantities of lactoferrin are found in human milk and this protein is thought to provide non-immune protection to the newborn through both anti-microbial and prebiotic effects (Lönnnerdal, 2003). Availability of commercial quantities of lactoferrin has allowed for supplementation of infant formula products to more closely match the composition of breast milk (Sawatzki, 1997; Williams, 2014). The scientific mechanisms associated with the anti-microbial effects of lactoferrin have been established (Farnaud & Evans, 2003). This information has provided a sound foundation for the use of lactoferrin-containing solutions in enhancing the safety of fresh food, notably in environments where microbial contamination is common (e.g., meat carcasses) (Naidu, 2002). Lactoferrin has also been shown to enhance immune function and to reduce allergic reactions (González-Chávez, Arévalo-Gallegos, & Rascón-Cruz, 2009), thus forming the basis for its application in specialist formula products, foods (e.g., yoghurt), personal care products, and immune support supplements. Lactoferrin also has potent bone growth stimulatory properties manifested through a dual mechanism – inhibition of osteoclasts and concomitant stimulation of osteoblasts (Cornish et al., 2004). Thus, lactoferrin may be helpful, when combined with other approaches, in preventing and/or treating osteoporosis.

Lactoperoxidase. The mechanism behind the anti-microbial action of lactoperoxidase has been established and forms the basis of applications for this bioactive whey protein (Boots & Floris, 2006; Kussendrager & van Hooijdonk, 2000). In particular, commercial quantities of lactoperoxidase have allowed for this protein to be used in a range of oral healthcare products (Boots & Floris, 2006; Jyoti, Shashikiran, & Subba Reddy, 2009). Clinical trials have shown that lactoperoxidase is efficacious in inhibiting bacteria associated with gingivitis, reducing inflammation and promoting the healing of gums, and reducing halitosis (Boots & Floris, 2006; Tenovuo, 2002). The anti-microbial properties of lactoperoxidase have also been exploited in toothpaste for young children so as to avoid the toxicity of fluoride prior to children learning not to swallow fluoride-containing toothpastes (Jyoti et al., 2009).

Immunoglobulins. These proteins are the most abundant of the established bioactive proteins found in bovine whey (Roginski et al., 2013; Smithers, 2008). When consumed, the immunoglobulins (IgG1, IgG2) impart passive immunity. Literature reports support their role in fighting infection, improving athletic

performance and recovery after exercise, improving the health of immuno-compromised patients, and enhancing gut health (Buckley, Abbott, Martin, Brinkworth, & Whyte, 1998; Hofman, Smeets, Verlaan, Lugt, & Verstappen, 2002; Korhonen, Marnila, & Gill, 2000; Mehra, Marnila, & Korhonen, 2006; Playford et al., 1999; 2000).

Growth factors. Mammalian cell growth factors, including insulin-like growth factor (IGF)-1, IGF-2, transforming growth factor (TGF)- β , platelet-derived growth factor (PDGF), fibroblast growth factor (FGF), betacellulin, and others (Roginski et al., 2013), have been isolated as a concentrated mixture from cheese whey, and characterised and commercialised (Belford et al., 1995; Francis et al., 1995; Pouliot & Gauthier, 2006; Raynor et al., 2000; Regester & Belford, 1999; Rowney et al., 2005; Smithers, 2004). This growth factor preparation shows (i) potent mammalian cell growth stimulatory activity, particularly for fibroblast cells (Belford et al., 1995); (ii) impressive wound healing effects (Raynor et al., 2000; Regester & Belford, 1999; Regester, Belford, West, & Goddard, 2003); (iii) the ability to protect against gut damage and address gastrointestinal disorders (Howarth et al., 1996; Playford, Macdonald, & Johnson, 2000); and (iv) efficacy in delaying the onset of mouth ulcers in an animal model of oral mucositis, a debilitating condition associated with chemo and/or radiation therapy of cancer patients (Clarke, Butler, Howarth, Read, & Regester, 2002).

Bioactive peptides. In addition to the inherent bioactivity of several of the whey proteins, their primary amino acid sequences contain peptides with bioactivity, additional to and often varied from that of the parent molecule (Roginski et al., 2013; Smithers, 2008). Perhaps the most carefully studied and commercially attractive peptides include (i) inhibitors of angiotensin I-converting enzyme (ACE); and (ii) potent anti-microbial agents. The ACE inhibitory peptides, derived by proteolytic digestion of α -lactalbumin and serum albumin (Korhonen, 2006; Pihlanto-Leppälä, 2000; Smithers, 2008), are effective in lowering hypertension and thus could play a role in enhancing cardiovascular health (Li, Le, Shi, & Shrestha, 2004). Proteolytic (pepsin, chymosin) digestion of lactoferrin results in the generation of a peptide fragment called lactoferricin that possesses potent anti-microbial activity (Bellamy et al., 1993; Gifford, Hunter, & Vogel, 2005; Smithers, 2008; Tomita, Wakabayashi, Yamauchi, Teraguchi, & Hayasawa, 2002). This peptide contains much of the N-terminal region of the parent molecule, and like lactoferrin is quite basic (Gifford et al., 2005). Lactoferricin retains much of the biological activity of the parent molecule and in some cases is more active, suggesting that the N-terminal region of lactoferrin is the area of the protein associated with the bioactivity (Gifford et al., 2005; Tomita et al., 2002). Lactoferricin has been shown to possess potent anti-microbial, including anti-fungal, and weak anti-viral activity, together with anti-tumour and anti-inflammatory effects (Bellamy et al., 1993; Gifford et al., 2005). Both the bovine and human variants of lactoferricin have been extensively studied, and while they are both highly positively charged peptides with similar spectrums of bioactivity, they do differ markedly in size, sequence and 3-dimensional structure (Gifford et al., 2005). The anti-microbial activity of both variants of lactoferricin appears to derive from their ability to form amphipathic structures, a feature they share with many other antimicrobial peptides (Bechinger & Lohner, 2006; Blondelle & Houghten, 1992). Because lactoferricin is readily generated by the action of pepsin on lactoferrin under acidic conditions, such as those found naturally in the human stomach, this whey peptide has particular relevance to human health.

Whey-derived lipids. The lipids associated with the milk fat globule membrane (MFGM) can be isolated from whey (Elías-Argote et al., 2013 and references therein). While the polar lipids, including glycerophospholipids and sphingolipids, represent less

than 1% of the total lipid material in the MFGM, they do possess important physico-chemical and biological properties (Dewittinck et al., 2008; Rombaut & Dewittinck, 2006). In the market, whey buttermilk powder is a rich source of polar lipids containing ~15% phospholipids on a dry basis (Jiménez-Flores & Brisson, 2008; Jiménez-Flores & Higuera-Ciapara, 2009). Phospholipids, including sphingomyelin, have been concentrated and isolated from whey using a combination of centrifugal, membrane-based and/or supercritical extraction techniques (Boyd, Drye, & Hansen, 1999; Costa, Elías-Argote, Jiménez-Flores, & Gigante, 2010; Dewittinck et al., 2008; Elías-Argote et al., 2013; Rombaut & Dewittinck, 2006; Walzem et al., 2002). Over the past 20 years, a number of bioactive effects have been ascribed to the MFGM and the constituent polar lipids, including anti-cancer, anti-microbial and antiviral effects, anti-hypercholesterolaemic activity, and the apparent suppression of some disease states like multiple sclerosis (Elías-Argote et al., 2013 and references therein). Notably, sphingomyelin has been shown to be effective in cancer pathogenesis and treatment (Elías-Argote et al., 2013; Lemonnier et al., 2003; Ogretmen & Hannun, 2004). While the biological activities of the MFGM and constituent lipids represent important traits in human health and nutrition, there has been little effort to date to incorporate these components into modern nutraceuticals or functional foods. Modern science is helping to better understand and characterise the MFGM and constituent lipids, including the importance of structure-function. This information will be critical in formulating products containing MFGM and the constituent lipids to ensure preservation of optimum structure, and thereby maximise the nutritional and functional benefits (Jiménez-Flores & Brisson, 2008).

Galacto-oligosaccharides. Lactose, the major whey solid, is an effective substrate in the production of galacto-oligosaccharides through the catalytic action of β -galactosidase, using either sweet or acid whey as the raw material (Fischer & Kleinschmidt, 2014; Splechtina et al., 2006; Torres, Gonçalves, Teixeira, & Rodrigues, 2010). In vitro, animal and human clinical studies have established the effectiveness of galacto-oligosaccharides as prebiotics (Torres et al., 2010). Together with the whey proteins and lipids, effective utilisation of lactose, notably its transformation into useful and valuable prebiotics, has been critical in the total valorisation of whey.

3.3. Globalisation and market sophistication

Milk production, transformation (including the production of whey and whey-based products) and trade are now global rather than regional activities (Ohlan, 2014). In this globalised dairy market, whey-based ingredients compete with many other ingredients (e.g., soy) for end product and market share. The desirable nutritional, functional and biological traits of whey ingredients, noted elsewhere in this review, has often positioned them as the high-quality and preferred ingredient option. However, competitors (e.g., soy protein and other vegetable protein ingredients) are gaining market traction through similar and complementary functionality at a much lower price-point (Day et al., 2006). In addition, many whey-based ingredients, once considered new, novel and 'value-added', have now moved into the 'commodity' category. Consequently, trade in these ingredients is now subject to the typical cyclical variation in global prices of commodities. WPC and, increasingly WPI, are ingredients that fall into this category.

The past 20 years have seen an increase in the sophistication of the global food marketplace. This transformation has been in response to consumer demands for safe, healthy, tasty and convenient foods and beverages (Weston, 2013). These consumer trends

and the drive toward health and wellness have created many and varied product openings and market opportunities for whey-based ingredients, built around their desirable properties. Notably, opportunities for whey ingredients in the sports nutrition arena have grown steadily over the past 10 years (Hoffman & Falvo, 2004; Mollica, 2012), supported by increasing scientific evidence for the benefits of whey proteins in muscle health (Paddon-Jones & Rasmussen, 2009; Reidy et al., 2013).

4. Tomorrow – challenges and opportunities

Science, technology and engineering have transformed the whey industry over the past approximately 50 years. The modern whey and whey products industry has much to be proud of, but challenges loom and more opportunities abound. While not wanting to be exhaustive or prescriptive, several of these challenges and opportunities are explored below.

4.1. Awash with acid whey – what are the options?

In some regions of the world, notably the USA, the unexpected market success of Greek-style yoghurt has created very large volumes of acid whey as a by-product of production. Greek-style yoghurt is now an industry worth >\$2 billion annually and this success is driving the construction of more factories for the manufacture of more yoghurt. While this success is to be celebrated by the industry, there is a more sinister side to the story. In New York State alone, >550 million L of acid whey is generated each year, and the volumes are growing (Elliott, 2013).

Whey from Greek-style yoghurt production is acidic (pH < 5.1) and often very acidic (pH < 4.5), and contains lactose and small amounts of protein (Table 1). The high BOD and low pH limit the options for further use and value addition of this acid whey. Some Greek-style yoghurt manufacturers are paying their milk suppliers to take back the acid whey, and these farmers are mixing it with silage for animal feed and a very small number (<0.5% of dairy farmers in New York State) are using it in anaerobic digesters for energy production (Elliott, 2013). Perhaps it is timely to explore value-added options for this ‘ocean of acid whey’.

Some value-added options for the utilisation of Greek-style yoghurt include: (i) an expanded anaerobic digester program to increase the number of participating dairy farmers and to perhaps create enough energy for both on-farm activities and to also feed into the state grid; (ii) isolation of valuable minor components (e.g., proteins, peptides) using high-throughput adsorption technologies such as chromatography with porous and acid-stable resins or membrane supports (Woonton et al., 2013); (iii) isolation of high-purity lactose using ion-exclusion technology (Hourigan et al., 2013); and (iv) production of galacto-oligosaccharides, for application as prebiotics, either directly from the acid whey, or indirectly from the isolated lactose (Fischer & Kleinschmidt, 2014).

A recent innovation in the production of Greek-style yoghurt promises to eliminate the generation of acid whey during the manufacturing process, and thereby remove the need for value-added options to treat the current large volumes of acid whey. This new process involves the use of proprietary Nutrilac® proteins from milk in the manufacture of Greek-style yoghurt with no apparent compromise on quality and taste, and the added benefit of zero acid whey (Despain, 2013; Foulds, 2014).

4.2. Improved efficiency and cost-effectiveness of processing

The global mega-retailers are creating ever increasing downward pressure on costs that flows through the food supply chain to include suppliers, processors and end-product manufacturers alike.

In this circumstance, the whey and whey products industry must continually explore and embrace new and novel processing options to remain cost-competitive. Recent cost-effective and improved efficiency processing options include (i) substituted stainless steel for enhanced production cycles, and improved cleaning efficiency and reduced cleaning frequency (Barish & Goddard, 2013); (ii) charged ultrafiltration membranes for improved concentration and fractionation of whey proteins (Arunkumar & Etzel, 2013; 2014); and (iii) non-thermal processing adjuncts (e.g., ultrasound) for production cycle and cleaning enhancements (Muthukumaran et al., 2005; 2007).

4.2.1. Efficiency and effectiveness of cleaning

Cleaning of stainless steel processing equipment represents a large cost to whey processors, and is estimated to account for as much as 15% of production time and 80% of production cost (Mauermann, Eschenhagen, Bley, & Majschak, 2009; Van Asselt & Weeks, 2013). Thus, reducing the frequency and improving the efficiency of cleaning would provide a very large economic benefit for whey processors. Fouling of plant (i.e., deposition of protein and minerals on the stainless steel surface) is influenced by operating conditions (temperature, flux), composition of the fluid being processed, and chemistry and topography of the surface of the processing equipment in contact with the liquid. The whey processor has limited flexibility with regard to operating conditions and negligible control over composition, but the chemistry and topography of the equipment surface can be addressed. Recent research from the University of Massachusetts has focussed on taking topographical and chemical approaches, many of which can be found in nature (e.g., lotus leaf, shark skin), to modification of the stainless steel surface so as to reduce foulant attachment and build-up. The chosen method involved stainless steel surface modification via an auto-catalytic nickel plating technique with co-deposition of fluoropolymer inclusions. The modified surface demonstrated remarkable non-fouling behaviour with dairy fluids, and was stable to the use of typical caustic cleaners and sanitisers (Barish & Goddard, 2013).

4.2.2. Efficiency and effectiveness of processing

Capturing future opportunities and accessing new markets for whey ingredients will be dependent on the ability to cost-effectively manufacture ‘tailored’ ingredients to meet the specific needs of each market (Schroeder, 2013). Cost-effective concentration and fractionation technologies, notably for whey proteins, will be critical in the manufacture of ingredients and products with the necessary characteristics to meet the demands of new and lucrative markets.

Modified ultrafiltration membranes. Recent research from the University of Wisconsin has resulted in the preparation and application of charged ultrafiltration membranes for (i) manufacture of WPC at high flux using negatively charged membranes (up to 4-fold higher flux than unmodified membranes); and (ii) fractionation of whey proteins using positively charged membranes, specifically the isolation of highly-enriched fractions of α -lactoglobulin and β -lactalbumin. While these two proteins are very similar in size, through the judicious use of pH and exploitation of slight differences in their isoelectric points, 1000 kDa modified membranes could be made highly selective in the separation of β -lactoglobulin from α -lactalbumin (Arunkumar & Etzel, 2013; 2014).

Ultrasonics. Non-thermal processing technologies, such as high pressure, pulsed electric field, and ultrasonics have for some years provided attractive alternatives to traditional thermal technologies for the preservation, safety and modification of dairy streams and components (Deeth, Datta, & Versteeg, 2013). Some of these same technologies, notably ultrasonics, have shown promise as non-

invasive approaches to improving the cost-effectiveness of dairy processing and the efficiency of cleaning. For example, in work from the University of Melbourne and collaborating partners, the simple application of ultrasound during ultrafiltration of whey led to production cycle improvements of up to 70% with no apparent detrimental effects on longevity of the ultrafiltration membranes (Muthukumar, Kentish, Stevens, Ashokkumar, & Mawson, 2007). Further, application of ultrasound improved the effectiveness and efficiency of cleaning membranes fouled by dairy (including whey) streams (Deeth et al., 2013; Muthukumar et al., 2005). The ultrasonics equipment can often be simply “bolted on” to existing processing plant, thus keeping the cost of implementation low, and making the ultrasonics-facilitated processing enhancements even more attractive to whey processors.

4.3. Embrace the unusual

4.3.1. Blended ingredients

End users of whey ingredients pay a premium for the nutritional and functional performance of these ingredients (Day et al., 2006). However, with increasing downward pressure on the costs associated with end products (see Section 4.2), whey and other dairy ingredients are coming under increasing competition from alternative ingredients. The latter include a number of both mainstream (e.g., soy, wheat) and fledgling (e.g., lupin, rice, pea) vegetable protein ingredients. While cost represents an important driver for the use of these latter sources of protein in place of whey-derived ingredients (Day et al., 2006), others include complementary functionality and health effects (Arrese, Sorgentini, Wagner, & Anon, 1991; Friedman & Brandon, 2001; Slavin, 1991), and potential allergies to bovine milk proteins (El-Agamy, 2007). For example, soy protein isolate and other soy-based ingredients are nowadays often used as alternatives to dairy (including whey) ingredients in a range of formulated foods (Riaz, 2006). Over the recent past, these soy protein ingredients have provided intense competition for whey protein products in a variety of applications where dairy once held pride of place (Bhatia & Greer, 2008). However, perhaps it's time to trade competition for partnership, at least in some areas of rivalry. For example, there is now compelling evidence that a blend of ‘fast’ (whey), ‘medium’ (soy) and ‘slow’ (casein) proteins provides substantial benefits in muscle recovery following resistance training (Reidy et al., 2013). Indeed, a proprietary blend of whey, soy and casein (TriSource™) is now being used in a variety of meal ‘power’ bars and sports nutrition products. Perhaps it is time to explore other potential applications for ‘fast-medium-slow’ protein blends (including dairy proteins partnered with soy, rice, lupin and/or pea), beyond their undoubted muscle health benefits, as the options are endless.

4.3.2. Non-bovine whey ingredients

The market for non-bovine milk and milk products (e.g., goat, sheep) has traditionally been small with much of the industry considered ‘cottage-style’. However, based upon many of the unique features of milk from sources other than cows, non-bovine milk and whey products are starting to gain momentum and to enter mainstream production and markets, although starting from a low base. Goat milk, for example, has some qualities closer to human milk than cows' milk (e.g., higher content of whey protein and ratio of whey:casein protein) (Ceballos et al., 2009). Goats' milk also has a higher content of calcium, magnesium and phosphorus, short-chain fatty acids, taurine, and conjugated linoleic acid when compared with cows' milk (Ceballos et al., 2009). The higher content of whey protein in goats' milk makes it an ideal candidate for the production of whey ingredients following the manufacture of goat cheese and other fermented products

(Ribeiro, 2010). Indeed, commercial production of goat WPC (65%) has recently commenced in The Netherlands (Goat Milk Powder – <http://www.goatmilkpowder.com/en/geiten-wpc/> (Accessed 10 October 2014)).

The ready availability of goat WPC will provide incentive for the manufacture of other (e.g., sheep) whey ingredients to further exploit compositional differences between non-bovine and cow milk (Raynal-Ljutovac, Lagriffoul, Paccard, Guillet, & Chilliard, 2008).

The unique compositional characteristics of non-bovine whey ingredients provide for new market opportunities and targeted applications, notably exploiting the similarities between goat and human milk composition. In particular, goats' milk is being used in infant formula products in China (Williams, 2014), and the availability of goat WPC will provide for further opportunities in this and related applications. For example, goat WPC is very rich in BCAAs and thus ideally suited to applications in muscle recovery after exercise (Reidy et al., 2013). There may also be market opportunities for blends involving goat WPC, regular bovine WPC, and vegetable protein sources (e.g., soy) for targeted applications in the health and wellbeing area.

4.4. New options for functional peptides

Whey has been established as a rich and unique source of functional and bioactive peptides, either naturally occurring or isolated from whey proteins through the targeted use of enzymes (Roginski et al., 2013; Smithers, 2008). The primary structure of whey proteins represents a ready and almost infinite source of peptides, and as such the isolation, characterisation and application of new and novel whey peptides have been active areas of research and development.

In a recent publication, a proline-rich whey peptide has been reported to stabilise milk proteins both with (75 °C or 100 °C) and without heat treatment (Selby-Pham et al., 2013). The peptide appears to limit α_{S1} -casein aggregation and enhance solubility of milk protein-containing powders over time, and shows a dose-dependent effect (Selby-Pham et al., 2013). This peptide would appear to have immediate commercial application with skim and whole milk powders, and milk protein concentrate (MPC) that tend to suffer from storage-related solubility problems that often relate to insolubility of the casein proteins over time (Anema, Pinder, Hunter, & Hemar, 2006).

Proline-rich whey peptides have also been reported to modulate the folding pathway of human amyloid- β peptide 1–42 into oligomers (Bharadwaj et al., 2012). Increased levels of the amyloid peptide and its self-associated aggregates are thought to be key events responsible for the progressive decline in cognitive function associated with Alzheimer's disease (Bharadwaj, Dubey, Masters, Martins, & Macreadie, 2009). The interaction of the proline-rich whey peptides with amyloid- β peptide 1–42 appears to interfere with the formation of anti-parallel β -sheet structures, disrupt the formation of oligomers, and lower cellular toxicity (Bharadwaj et al., 2012). This exciting discovery could play a role, together with other strategies, in addressing the growing problem of dementia in the elderly.

5. Conclusions

Man's involvement with dairy whey has come full circle. From a fluid revered for its medicinal properties in the 17th, 18th and 19th centuries, to a troublesome waste by-product of an expanding dairy industry in the first half of the 20th century, to nowadays a valuable raw material containing a vast array of useful and valuable components and their derivatives.

Expanding science knowledge about the components in whey, their characteristics and useful properties has played a pivotal role in the transformation of whey into a co-product of great value to the global dairy industry. In parallel with greater science knowledge about whey have been advances in processing technology to allow for the cost-effective and efficient manufacture of whey components as ingredients and their modification into many more ingredients.

Availability of industrial quantities of whey proteins, peptides, lactose, and lipids has allowed for commercial applications in foods, specialised formulations, bio-medical products, pharmaceuticals, and cosmetics in a marketplace that shows sophistication and craves the nutritional, functional and biological traits of whey ingredients. Detailed science knowledge of whey components, notably the proteins, has also helped troubleshoot problems and established whey ingredients as reliable performers in a vast array of applications.

The whey industry is currently enjoying great success, but new challenges present on the horizon and opportunities abound. Examples include the vast volumes of Greek-style yoghurt acid whey, downward pressure on the cost of manufacturing whey ingredients, competition from other ingredients for market share, and exciting possibilities in the area of functional whey peptides. These looming challenges will be addressed and opportunities captured through science and technology options, thus ensuring that the industry continues to have a bright future.

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