Symposium review: The dairy matrix—Bioaccessibility and bioavailability of nutrients and physiological effects*

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ABSTRACT

Several studies have linked food structure and texture to different kinetics of nutrients delivery. Changes in some nutrients' release rate, such as proteins and lipids, could induce different physiological effects (e.g., satiety effect, reduction of postprandial lipemia). Recently, experts are proposing to consider the food as a whole instead of looking at specific nutrients, as the combination of food components and the way they are structured could change their physiological effects. This review highlights recent knowledge linking the different levels of structure of dairy products to their digestion, absorption, and physiological effects. Two examples, yogurt and cheese, will be presented to showcase the contributions of dairy food structure to nutrient release rates. One study aimed to validate whether changes in the casein:whey protein ratio or addition of fiber could influence the digestion kinetics of protein and, subsequently, satiety. A static *in vitro* digestion model has been used on experimental yogurts differing by their casein:whey protein ratio or dietary fiber content. A human trial with healthy men ($n = 20$) consuming 5 isocaloric and isoproteinemic yogurt snacks before monitoring lunch intake revealed that the yogurt formulation with increased whey protein content significantly reduced subsequent energy intake compared with its control. This result was linked to slower *in vitro* disintegration rate and soluble protein release for yogurts with increased whey protein, whereas no difference was observed for yogurts with fiber. A second study allowed discrimination between the effects of cheese attributes on lipid release and absorption. Nine commercial cheeses were digested *in vitro*, and 2 were selected for

the *in vivo* study, in which plasma concentrations of triglycerides (TAG) were followed before and after meal consumption. The *in vivo* study revealed that cream cheese, but not cheddar, induced a greater increase in TAG concentrations at 2h than did butter; this difference was linked to their *in vitro* disintegration. These studies demonstrate that the dairy food matrix *per se* modulates foods' nutritional properties. Other studies recently published on this topic will also be included, to put in perspective the important role of the dairy food matrix on release of nutrients and their physiological effects, and how this can be compared with other foods.

Key words: dairy product, digestion, postprandial lipemia, satiety

INTRODUCTION

Food is a daily topic in the population for various reasons. Food is our everyday fuel, having a fundamental role in providing essential nutrients. However, cultural, behavioral, and emotional motives are involved when mealtime comes. The role of diet and food in several societal challenges induces some questioning—for example, on the environmental impact of the food we consume. Multiple factors are involved in sustainability, and the concept is often oversimplified. The FAO has defined a sustainable diet as “protective and respectful of biodiversity and ecosystems, culturally acceptable, accessible, economically fair and affordable; nutritionally adequate, safe and healthy; while optimizing natural and human resources” (Burlingame and Dernini, 2012). Among others, questions are raised about nutritional food safety. From an approach based on nutrients implemented to reduce deficiencies and associated diseases, the world now faces an epidemic rise of overweight and obesity-associated higher risks of chronic diseases. It has recently been reported that 22% of deaths worldwide were related to dietary risks, mostly from cardiovascular diseases (GBD 2017 Diet Collaborators, 2019). Which diet is the safest? Are there foods to avoid? The consumer is confused with all the contradictory information communicated continuously.

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Approaches based on the effects of individual nutrients and instructions to avoid some, such as saturated fat, sugar, and cholesterol, have been difficult to translate to the public (Mozaffarian and Ludwig, 2010). From the failure of interventions based on the nutrient content of foods, a growing number of researchers are suggesting a new approach that takes into consideration the food format instead of the nutrients that compose it. This would be better, to favor adoption of a healthy diet and reduction of the risk of chronic diseases (Mozaffarian and Ludwig, 2010). However, the idea that foods should be considered as more than the sum of their nutrients is recent (Jacobs and Tapsell, 2007; Turgeon and Rioux, 2011, 2015; Thorning et al., 2017; Aguilera, 2018; Moughan, 2018). Several research teams have provided evidence that dairy products should be considered as a whole when looking at their nutritional and physiological effects (Turgeon and Rioux, 2011, 2015; Thorning et al., 2017; Fardet et al., 2019).

Dairy products have historically been consumed in many parts of the world for their richness in nutrients. However, over the years some questions have been raised about the influence of dairy lipids on health. Several decades ago dairy SFA content was flagged for possible contribution to increased risk of cardiovascular diseases (Keys et al., 1986). In the last decade, numerous studies have counterbalanced this statement (Siri-Tarino et al., 2010; Dehghan et al., 2018) and several meta-analyses and overviews concluded that consumption of dairy products with either regular or low fat content has no adverse effect on the risk of cardiovascular disease (Drouin-Chartier et al., 2016a, b; Fontecha et al., 2019). However, identification of the favorable factors explaining a different outcome of saturated fat in dairy products on health compared with other sources of saturated fats continues to be an open research question. In this paper, 2 case studies are presented to highlight how dairy products matrices and their properties could affect nutrients' digestion, absorption, and physiological effects. This paper does not aim to be an exhaustive review, and readers are referred to recent detailed reviews for further reading (Thorning et al., 2017; Fardet et al., 2019; Michalski et al., 2019).

MILK AND DAIRY PRODUCTS: A COMPLEX MATRIX

Milk has evolved as a uniquely mammalian adaptation to provide the immunological protection and the whole nutrients and energy required to sustain the physical growth and advanced cognitive development of offspring during the first months of life. Such a highly nutritious delivery system can only be achieved through the unique structuration and organization of each of

the main constituents of milk, such as lipids, proteins, carbohydrates, minerals, and other minor components, in a manner to be optimally digested and metabolized by the newborn. The levels of assembly of the milk macronutrients markedly influence their digestion and assimilation along the gastrointestinal tract.

At the macroscopic level, milk is an oil-in-water emulsion formed by small milk fat globules dispersed in a serum phase. At the microscopic or colloidal level, the casein micelles, globular proteins, and lipoprotein particles are in suspension within a solution rich in lactose, soluble proteins, minerals, vitamins, and other minor components. Among these structural organizations, milk fat is considered one of the most complex of all natural fats. It contains about 400 different fatty acids (Månsson, 2008) esterified to triacylglycerol (**TAG**) and surrounded by a natural membrane, the milk fat globule membrane, composed of a variety of polar lipids (phospholipids and sphingolipids) and proteins (Mather, 2000; Lopez, 2011). This complex structure finds its origin in the milk fat globule secretion inside and their excretion outside the lactating cells (Keenan, 2001). The milk fat globule membrane not only allows the milk emulsion to stabilize by surrounding the immiscible TAG into small spherical fat droplets but also facilitates their digestion and assimilation by the newborn, promoting gut immunity as well as cerebral development (Timby et al., 2014; Bourlieu et al., 2015; Bhinder et al., 2017; Le Huërou-Luron et al., 2019).

Milk proteins are considered to be among the highest-quality proteins, due to their high proportion of essential amino acids and excellent digestibility. Caseins compose about 80% of the total milk proteins. They exist as large colloidal aggregates, known as casein micelles. The casein micelle supramolecular structure is still an object of debate, but most models agree that κ -casein must be located on the surface of the micelle, particularly because of its stabilizing role, its accessibility to chymosin hydrolysis, and the formation of complexes with denatured serum proteins upon heat treatment (de Kruif et al., 2012; Holt et al., 2013). Several major interactions come into play in maintaining the internal micellar structure, including the interaction between phosphoserine residues of casein molecules and the presence of calcium phosphate "nanoclusters" and casein-casein interactions (hydrophobic, hydrogen, electrostatic; de Kruif et al., 2012). Because of its unique colloidal structure, the casein micelle allows the transport and delivery of proteins and minerals to the mammal's offspring. The remaining milk proteins are the whey proteins, mostly comprising β -lactoglobulin (50% of soluble proteins), α -lactalbumin (20%), and serum albumin (10%). These globular proteins are more sensitive than caseins to thermal denaturation and ag-

gregation, changing the properties of milk (Mulvihill and Donovan, 1987).

Dairy processing induces important modifications to these complex milk structures. Controlling these structural changes allows the production of a large variety of dairy products, such as butter, cheese, and yogurt. These complex dairy matrices are obtained by adjusting the conditions of pH or ionic strength, adding salt (mono or divalent cations) or enzymes, or applying physical (thermal treatment, homogenization, evaporation, drying) or mechanical (homogenization, churning, pumping) treatments.

Table 1 presents selected dairy products based on their structure and composition in lipids, proteins, and calcium. Most of these dairy products are oil-in-water emulsions, except for butter, which is a water-in-oil emulsion. Butter is obtained by cream churning, resulting in a fat phase inversion and the formation of water-in-oil emulsion, characterized by a partially crystallized TAG phase within which small serum droplets are entrapped. For cheese, the milk fat is embedded either as small fat droplets or as unstructured liquid fat dispersed in a coagulated casein network. Milk fat globules are entrapped within the casein matrix, contributing to the elasticity and hardness properties of the cheese. Similar to yogurt, cheese made from acid coagulation is very loose, soft, and high-moisture. Acidification causes a destabilization of the casein micelles through the dissociation of the colloidal calcium phosphate (Lucey, 2016). Moreover, the hairy polar layer of κ -casein at the surface of the micelle collapses, and the charge repulsions decrease as the pH move closer to the casein isoelectric point (pH 4.6). These changes favor protein-protein association via hydrophobic interactions and the formation of a 3-dimensional gel network of aggregated caseins (Lucey, 2016). On the other hand, rennet coagulation results in a firmer and more tightly knitted casein network. Indeed, as the chymosin hydrolyzes the κ -casein hairy polar layer at the surface of the micelle, the decrease of the micelle surface repulsions promotes their aggregation in the presence of ionic calcium and the buildup of a firm coagulum. Therefore, the level of calcium mineralization within the cheese matrix will also greatly affect its texture. As seen in Table 1, the texture of the gelled network is semi-solid at lower concentrations of calcium (cream cheese, Camembert), solid or viscoelastic at intermediate concentrations (Cheddar), and very hard at higher concentrations (Parmesan). In yogurt, the oil-in-water emulsified fat droplets are dispersed in a loose protein gelled matrix obtained by acid coagulation by fermentation. Set yogurt can be stirred by mechanical action, causing a partial breakdown of the semi-solid casein network and a loss in viscosity. On the other hand, Greek yogurt

is obtained by increasing the protein concentration, originally by straining but nowadays by ultrafiltration (UF) or protein fortification before acidification or by centrifugation or UF of the acid coagulum. Increasing the casein content allows for extensive formation of weak hydrophobic interactions between and within casein aggregates in a more tightly packed gel network, increasing the product viscosity and smoothness.

TWO CASE STUDIES TO EXPLORE THE LINK BETWEEN DAIRY STRUCTURE AND PHYSIOLOGICAL EFFECTS

The last decade has seen an exponential number of publications reporting studies on food digestion using *in vitro* systems, either static or dynamic (Egger et al., 2016, 2019). Static digestion systems are simple to use and to implement at low cost but may present large interlaboratory variations in operating conditions. A protocol has been published from an international consensus, describing experimental conditions simulating human digestion on the basis of physiological inferred conditions (Egger et al., 2016; Brodkorb et al., 2019). Static digestion allows performance of a large number of experiments, and it may be considered a good screening method or a methodological approach to study specific phenomena (matrix disintegration under digestion conditions, release of specific nutrients, hydrolysis, and others). However, it is acknowledged that the results have to be validated with *in vivo* studies, the gold standard being human studies. The physiological relevance of *in vitro* data has been appraised for various macronutrients, micronutrients, and phytochemicals (Egger et al., 2019; Bohn et al., 2018). Comparison of *in vitro*–*in vivo* outputs (protein hydrolysis rate, profile of peptides produced) at the end of gastric and duodenal digestions were considered comparable. However, most of these systems were simple and involved individual proteins or model matrices (milk and rennet or acid gels, for example). Several bioactive peptides were found in both *in vitro* digestion and animal and human digests, considered a sign of representativeness of digestive models. Lipid results were assessed from selected studies on emulsions. *In vitro*–*in vivo* correlations were reported between the rate of fatty acid release and the plasma-TAG profile, showing a slower *in vitro* lipolysis and appearance in plasma that depended on fat coalescence (Golding et al., 2011). However, changes in the structuration of lipids (the mechanism of breakdown) in the stomach may have a strong influence on the correlation with physiological events, as it affects gastric emptying. Usually, once released from a solid matrix in the stomach by the action of the acidic gastric pH and pepsin, lipids

Table 1. Composition, characteristics, and in vitro digestibility of selected dairy products¹

Dairy product	Protein ² (g/100 g)	Lipid ² (g/100 g)	Ca ² (mg/100 g)	LAB	Matrix characteristics ³	Textural properties	Digestibility ⁴ (% gastric MDI)
Butter, salted	0.9	81.1	24	No/Yes ⁵	Continuous lipid phase (water in oil emulsion)/residual traces of MFGM	—	100
Cheese (Camembert)	19.8	24.3	388	Yes	FG/aggregates/free fat	Semi-solid	66–76 ⁶
Cheese (Cheddar)	24.0	33.8	675	Yes	FG/aggregates/free fat	Solid/viscoelastic	25–43 ⁷
Cheese (cream cheese)	5.9	34.2	98	Yes	Homogenized milk FG/potential fragments of MFGM	Semi-solid	NA
Cheese (Parmesan)	35.8	25.8	1184	Yes	FG/aggregates/free fat	Solid	NA
Cream (35% MF)	2.1	35.0	66	No/Yes ⁸	Native FG/homogenized milk FG/potential MFGM fragments	Liquid	NA
Milk (whole, 3.25% MF)	3.2	3.3	113	No	Native FG/homogenized milk FG/potential MFGM fragments	Liquid	100 ⁹
Yogurt (plain, 2 to 3.9% MF)	4.6	2.0	147	Yes	Native FG/homogenized milk FG/potential MFGM fragments	Gel/viscoelastic	100 ⁹

¹MFGM = milk fat globule membrane, FG = fat globule, LAB = lactic acid bacteria, MF = milk fat, NA = not available.

²Retrieved from Health Canada (2015).

³Based on the study by Michalski et al. (2013).

⁴MDI = matrix degradation index; determined at the end of gastric digestion, using an in vitro model adapted from Versantvoort et al. (2005).

⁵Depending on the processing method used.

⁶Fang et al. (2016a).

⁷Lamothe et al. (2012).

⁸Depending on the type of cream (sour or cultured cream may contain LAB).

⁹Lamothe et al. (2017).

can be dispersed and reorganized as oil-in-water emulsified droplets by the gastric movements, increasing their accessibility for gastric lipase and lipolysis. Here, in a recent review Bohn et al. (2018) concluded that more in vitro–in vivo research is required, especially on complex food systems in which each digestion step may impart modification in the structure and interactions between nutrients that may be more difficult to mimic in vitro.

Case Study 1: Protein Digestion in a Yogurt Matrix and Relationship with Satiating Effect

The satiating role of protein has been recognized and investigated, to reduce overconsumption due to hunger and influence the energy balance (Westerterp-Plantenga et al., 2012; Chambers et al., 2015; Morell and Fiszman, 2017). Both quantity and protein type have been reported to affect food intake and metabolism (Morrison and Laeger, 2015). Several products rich in protein have been studied, including high-protein yogurts (14 to 24 g per serving), which efficiently influenced appetite sensations and reduced subsequent food intake (Douglas et al., 2013; Ortinau et al., 2014). These products have a higher protein content than what is found in standard

commercial products, which is about 4% total protein content. One might wonder whether protein enrichment is needed to induce a significant satiating effect. This was the context of a study aiming to evaluate the effects of yogurt formulations with equivalent caloric and protein contents consumed as a snack on appetite sensations and food intake at a subsequent ad libitum buffet-type lunch (Doyon et al., 2015). Each portion of yogurt (120 g) provided a fixed amount of protein (4.5 g), with some formulations including fibers (inulin or β -glucan). One formulation had a higher whey protein content, with a casein-to-whey protein ratio of 1.5 compared with 2.8 for commercial samples. No differences were observed among the yogurt formulations for any of the appetite sensation ratings as recorded by visual analog scales, for either glucose or insulin profiles (240 min after breakfast). However, energy intake at lunchtime was significantly reduced (812 kJ) when the proportion of whey protein was increased compared with the control (from 1.14g in the control to 1.57g of whey protein, total protein content was 4.50 g). Interestingly the reduction in food intake was higher than the caloric contribution of the yogurt eaten as a snack. The question raised by these results is how a change in

casein-to-whey protein ratio can induce this difference in satiating effect?

Several factors may interplay. First, protein type has to be considered. Whey proteins have a documented high satiating effect (Luhovyy et al., 2007) and could mediate satiety hormones (Chungchunlam et al., 2015). Differences between caseins and whey proteins during digestion have been studied and have led to the introduction of the concept of “fast” and “slow” proteins due to the different rates of leucine appearance in serum after consumption. Caseins were qualified as slow proteins because they form a clot in acidic stomach conditions (Boirie et al., 1997). This can hinder enzyme access to the substrate and delay gastric emptying, resulting in a delayed appearance of amino acid in blood serum. Conversely, whey proteins were more rapidly digested and emptied into the duodenal compartment to be further hydrolyzed and absorbed. Another factor to consider is the processing steps, as heat treatment can influence the yogurt matrix structural characteristics and its behavior during digestion. Recently, it was shown that coagulation during gastric digestion was influenced by heat treatment affecting the gastric emptying rate and the metabolic response (Mulet-Cabero et al., 2019). Mulet-Cabero et al. (2019) showed that heat treatment affects the consistency of the coagulated milk proteins in the stomach, with a more fragmented coagulum obtained for heat-treated milks. The severity of the treatment also affects proteolysis, as a higher digestion of milk proteins was observed in UHT milk. A heat-treatment of 90°C/4min is commonly applied to milk formulation during yogurt making, as this favors denaturation of whey proteins and their interactions with casein micelles, to improve water retention ability and decrease serum separation during storage. In a previous study, higher whey protein content (casein: whey protein ratio 1.5:1) showed higher levels of protein denaturation and more viscous gastric digested samples (Rioux and Turgeon, 2012). The *in vitro* digestion behavior of the yogurts used in the clinical trial revealed higher residual contents of insoluble solids (mainly proteins) at the end of the gastric digestion for the 1.5:1 ratio. The lower accessibility of aggregated whey proteins during gastric digestion may affect *in vivo* gastric emptying and satiety. As we mentioned in our study (Rioux and Turgeon, 2012), other factors may also influence digestion behavior and satiety, such as the presence of other ingredients—for instance, lipids (not a variable in this study) or fiber (no difference induced by inulin or β -glucan in this study)—or differences in viscosity or palatability of the product. Recent studies have also pointed out possible indirect effects of whey proteins on gut microbiota and on nutrient

absorption within the intestine that could affect energy absorption, as whey proteins influence adiposity and the hypothalamic control of energy balance (McAllan et al., 2015; Nilaweera et al., 2017).

To summarize, many factors may influence protein digestion, considering their structural features at different scale lengths from the macroscopic, to the microscopic, and to the molecular scale: protein composition (such as the casein:whey protein ratio) and conformation, level and strength of interactions and protein aggregation, and behavior in gastric conditions. Digestion requires breakdown of yogurt's 3-dimensional semi-solid network. Viscosity in the stomach may affect diffusion rate of the enzyme to reach its substrate. For solid food, an additional step to disintegrate the structure may delay protein hydrolysis. This food matrix effect may be illustrated using cheese as an example of a dairy product that ranges from a semi-solid to a hard matrix. Food matrix disintegration generally depends on initial food properties, disintegration rate, and residence time (Bornhorst et al., 2015). In a series of papers, our team examined *in vitro* digestion of various cheese types (Lamothé et al., 2012; Ayala-Bribiesca et al., 2016; Fang et al., 2016a, b; Guinot et al., 2019). Disintegration during *in vitro* gastric digestion was different among the different types of cheeses. However, once transferred to duodenal conditions, digestion was fast and resulted in extensive hydrolysis, corresponding to an expected good protein bioavailability. Each cheese variety possesses a specific microstructure dependent on its composition (protein, fat, mineral, and water content), its microbial ecosystem, and the process used (homogenization, pressing, temperature) during each individual cheese production step. Microstructure explains individual textural properties of cheeses, and this was correlated with cheese matrix disintegration that increases lipid access to lipase, increasing FA release. Comparing the digestion of Camembert cheese, smear cheese, young Cheddar, aged Cheddar, and Mozzarella, disintegration was inversely correlated with hardness, cohesiveness, and chewiness of cheeses (Fang et al., 2016a). Different disintegrations were associated with distinctive degrees of proteolysis and different peptide profiles. Comparison of cheeses with similar textural attributes, such as regular and low-fat Cheddar and Mozzarella cheeses, showed that compositional attributes were the main factors correlated with disintegration after the gastric step. Higher fat content of cheese was correlated with higher gastric disintegration (Fang et al., 2016b). Experiments performed without enzymes highlighted specific soaking and shearing effects during digestion. Up to 30% cheese disintegration was observed at the end of duodenal digestion, compared with 72% in the

experiments with enzymes. Another design performed to study lipid release included a wider range of cheese categories, such as cream cheeses (homogenization step) and parmesan (higher hardness; Guinot et al., 2019). In these cases, gastric disintegration was better predicted by textural attributes such as fracturability, springiness, cohesiveness, and hardness (from penetrometry tests). Another in vitro–in vivo protein study, using mini-pigs as a model, also endorses the effect of dairy matrix on physiological responses induced by acidic and rennet gels (Barbé et al., 2014a, b). More work is needed to continue to isolate food matrix features that can trigger physiological responses.

Case Study 2: Lipid Appearance in Serum After Ingestion of Different Cheeses and Butter

Consumption of dairy lipids and their potential effects on physiological responses and long-term effects on health have been and continue to be the object of active research since the 1980s (Gillis et al., 2018; Michalski et al., 2019). Several research angles are used to better understand and isolate variables, explaining their physiological influence. Acute postprandial responses such as lipemia are gaining interest, as Bansal et al. (2007) observed a strong association of postprandial TAG concentrations measured at 4 h with cardiovascular disease risk. Prolonged high lipemia may overexpose arteries to TAG-rich lipoproteins (Vors et al., 2014), which should be avoided. Could acute responses help us understand why cheese consumption has a neutral or favorable effect on cardiovascular risks despite its saturated fat content? To investigate a possible matrix effect, a randomized, crossover and controlled trial postprandial study was designed, to measure lipemia after a breakfast including dairy fat of different structures: soft cream cheese (emulsified dairy fat in a semi-solid matrix), cheddar cheese, and butter (Drouin-Chartier et al., 2017). Care was taken not to alter the dairy matrix structure before consumption. After 2 h, TAG levels significantly increased for subjects who consumed the cream cheese meal compared with the cheddar cheese meal, although the opposite is seen after 6 h. All meals had a similar lipemia at 4 h. The lower apoB-48 incremental area under curve observed with cream cheese may correspond to lower and smaller chylomicron secretion. These differences induced by the cheese matrix show that it can modulate postprandial lipemia. In vitro digestion performed on the same cheese samples showed that cream cheese disintegration is fast and almost complete after 2 h of gastric digestion, whereas cheddar disintegration is incomplete at the same time point (less than 55%; Guinot et al., 2019). Emulsified

fat droplets in cream cheese were readily available for lipolysis (Vors et al., 2013). On the other hand, limited disintegration of the cheddar cheese matrix is in accordance with other in vitro studies, in which disintegration was found to range between 25 and 43% after 2-h gastric digestion (Lamothe et al., 2012; Fang et al., 2016b). Fat droplets are embedded in a solid cheese matrix, which must be disintegrated to allow lipolysis. Textural parameters such as springiness and cohesiveness are negatively correlated with disintegration at the end of the gastric digestion stage, whereas capacity to fracture was positively correlated (Guinot et al., 2019).

Another example of the influence of matrix properties on lipemia is the effect of the length of the FA carbon chain of the fat fraction used for cheese manufacture. A recent animal study was performed with cheddar cheeses manufactured with 2 fat fractions (olein or stearin) that have different melting points and 2 calcium levels (Ayala-Bribiesca et al., 2018). Cheeses made with the solid fat fraction (stearin, with a melting point of 42.3°C) were harder to disintegrate, which delayed lipolysis and overall fatty acid bioaccessibility compared with the cheese made with the liquid fat fraction (olein, with a melting point of 34.7°C; Ayala-Bribiesca et al., 2017, 2018). The mass fraction of unabsorbed fatty acids recovered from rat feces in the test was higher in the stearin meal compared with that of the olein meal. Calcium content is an important factor for lipid bioavailability, as fat may form insoluble calcium soaps with long-chain saturated FA in the duodenal environment (Graham and Sackman, 1983). Calcium interaction with these fatty acids also contributes to removing them from the fat droplet surface and reducing an inhibitory effect on lipase due to fat accumulation (Hu et al., 2010). In cheese (Ayala-Bribiesca et al., 2017), calcium has been shown to interact with long-chain fatty acids (stearin) to produce Ca soaps, but the authors of the study observed no interaction with shorter fatty acids such as olein. The removal of long-chain fatty acids trapped by the production of Ca soap counteracts their accumulation at the oil–water interface, which would otherwise hinder the lipolytic activity of lipase.

Study of the role of the cheese matrix on its digestion and postprandial responses is part of understanding the long-term health effects associated with cheese consumption. Several factors have to be considered in lipid digestion, and Figure 1 schematizes those identified in recent publications (Li et al., 2011; Lamothe et al., 2012; Michalski et al., 2013, 2019; Vors et al., 2013; Ayala-Bribiesca et al., 2016, 2018; Fang et al., 2016a; Thorning et al., 2017; Michalski et al., 2019). In addition to composition and textural properties, more work is needed to consider the effect of the microbial

Figure 1. Main factors affecting cheese matrix texture, digestibility, and physiological effects.

ecosystem specific to cheese varieties with the production of specific metabolites and bioactive compounds in cheese.

CONCLUSIONS

The aim of this review was to shed some light on the effects of dairy matrices on milk constituents' nutritional attributes and physiological effects. In vitro approaches are useful to model specific phenomena and study large number of parameters before getting into animal or human trials. These models allow precise control of digestion parameters such enzymatic conditions, pH, and temperature, but they lack the ability to reproduce some physiological events, such as gastric emptying. More studies are required for complex and widely consumed food such as cheese. Considering the large number of parameters to account for, such as the large range of composition, processes, and structures, more studies linking in vitro and in vivo results are needed. Dairy products also naturally contain a variety of bioactives, including peptides, minor lipids, and oligosaccharides, as well as a complex microbial ecosystem. These must be investigated to unravel some

specific physiological effects of dairy products. For example, we showed that protein digestion of a yogurt matrix is affected by the casein: whey ratio and the protein conformational changes sustained during manufacturing, all of which affect energy intake and satiety. The protein structural organization of different types of cheeses affects their texture, which, in turn, determines the extent of matrix disintegration and proteolysis. By contrast, postprandial lipemia is affected not only by specific lipid composition and its level of organization but by the dairy matrix structure and textural properties, as shown through the example of hard versus soft cheeses. Finally, this evidence supports the need for researchers to go further into complexity and even include meals in their studies, because this is closer to real life, and specific combinations could reduce or exacerbate release of nutrients, their absorption, and their metabolic fate.

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