Overview: the food matrix and its role in the diet

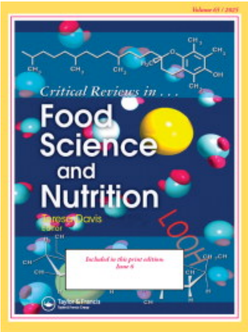
Article

Published Version

Weaver, C. M. ORCID: https://orcid.org/0000-0002-5450-9609 and Givens, D. I. ORCID: https://orcid.org/0000-0002-6754-6935 (2025) Overview: the food matrix and its role in the diet. Critical Reviews in Food Science and Nutrition. ISSN 1549-7852 doi: 10.1080/10408398.2025.2453074 Available at https://centaur.reading.ac.uk/120904/

To link to this article DOI: http://dx.doi.org/10.1080/10408398.2025.2453074

Publisher: Informa UK Limited



Critical Reviews in Food Science and Nutrition

ISSN: (Print) (Online) Journal homepage: www.tandfonline.com/journals/bfsn20

Overview: the food matrix and its role in the diet

Connie M. Weaver & D. Ian Givens

To cite this article: Connie M. Weaver & D. Ian Givens (04 Feb 2025): Overview: the food matrix and its role in the diet, Critical Reviews in Food Science and Nutrition, DOI: 10.1080/10408398.2025.2453074

To link to this article: https://doi.org/10.1080/10408398.2025.2453074

Published online: 04 Feb 2025.

CRITICAL REVIEWS IN FOOD SCIENCE AND NUTRITION
https://doi.org/10.1080/10408398.2025.2453074

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

OPEN ACCESS Check for updates

Overview: the food matrix and its role in the diet

Connie M. Weaver[a] and D. Ian Givens[b]

[a]School of Exercise and Nutritional Sciences, San Diego State University, San Diego, California, USA; [b]Institute for Food, Nutrition and Health, Earley Gate, University of Reading, Reading, UK

ABSTRACT
The food matrix which includes the physiochemical structure and interaction with chemical constituents is a focus of investigation that is revealing potentially important influences on diet and health. This paper, the first in an article collection titled, The Important Role of the Dairy Matrix in Diet and Health, serves as an introduction to the food matrix to put into context the subsequent articles specific to the matrix effects of dairy milk, cheese and yogurt on human health. This introductory article describes the effects of processing on the food matrix and implications for diet and health, examines the contribution of nutrients compared to whole foods and food patterns, and characterizes examples of the complexity of the food matrix including current controversies of dairy fat and ultra-processed foods. The gaps in knowledge and research identified in this overview may help guide researchers and funding entities moving forward. Current knowledge indicates that translating research on the food matrix to the consumer through recommendations for the intake of whole foods and food patterns is prudent at this time.

KEYWORDS
Matrix; Dairy; Nutrition; Diet; Health

Introduction: what is the food matrix?

Understanding the role of diet in health has moved past the nutrient profile of the food, meal, or diet. Advances in technologies have allowed us to think in the broader context of food patterns and the food matrix. The food matrix is not only the composition of nutrients, bioactive constituents, and other compounds present but also how they are packaged and compartmentalized. It reflects the processing that the product has undergone, including changes in physical state of the product, altered endogenous constituents, and addition of inert and live chemicals or microorganisms (Aguilera 2019). This overview, an introduction to the special article collection titled, "The Important Role of the Dairy Matrix in Diet and Health" will explore how the complex nature of the food matrix influences diet and health outcomes in various ways and how we can understand health benefits through the lens of the food matrix. The food matrix that has been the most studied is dairy and several papers have already been written on this particular food matrix (Weaver 2021; Thorning et al. 2017). This special article collection includes papers that provide deeper insights into the milk, yogurt and cheese matrices and their potential impact on consumer health. To give context to the subsequent articles focused specifically on the dairy matrix, this overview will introduce the many nutritional components in food where the matrix may influence diet and ultimately health. This overview is not meant to be comprehensive. Indeed, the evidence for matrix effects on health outcomes is still developing. A few examples of currently hot topics of debate will be elaborated upon to illustrate the importance of investing in research on the food matrix to better understand the role of food and processing in diet and health.

Effects of processing on nutrient content, bioavailability of nutrients and bioactive components, and implications for health

The food matrix: the importance of physical form and structure

Whilst it has been known for a long time that foods are complex mixtures of nutrients sitting within a range of physical structures, knowledge on the impact of these matrices on the nutritional and subsequent health characteristics of the food has been limited. Because of this Mulet-Cabero et al. (2024) described the need for harmonizing definitions to assist in understanding the literature on the food matrix and its impact. They proposed a definition for the dairy matrix as "describing the unique structure of a dairy food, its components (e.g., nutrients and non-nutrients), and how they interact." They also defined dairy matrix health effects as "referring to the impact of a dairy food on health that extends beyond its individual components." It is likely that these statements could equally apply to many nondairy

CONTACT Connie M. Weaver cmweaver@sdsu.edu

foods. Examples of the importance of form and structure of the matrix in relation to fruit were given by Haber et al. (1977) and recently by Crummett and Grosso (2022). Haber et al. (1977) fed test meals containing 60 g of carbohydrates to healthy subjects based on intact apples, fiber-disrupted apple purée and apple fiber-free juice. Postprandial plasma glucose increased to similar concentrations in all three treatments, but serum insulin rose to a higher concentration following the juice and purée than the intact apples. It was concluded that physical disruption of the fiber can lead to disturbed glucose homeostasis due to inappropriate insulin release.

Crummett and Grosso (2022) highlighted that whilst increased dietary fiber intake is associated with reduced postprandial glycemic response, less is known whether physically disrupted fiber modifies this response. They compared the glycemic response in healthy students of consuming whole fruit (190 g apple, core and seeds removed, and 148 g of blackberries) compared with blended fruit. They found that the postprandial maximum glucose concentration (whole 42.5 ± 4.6; blended 28.8 ± 2.4 mg/100 ml, $p = 0.004$) and glucose incremental area under the curve (whole 1269 ± 124; blended 850 ± 109 mg*min, $p = 0.005$) were significantly lower in blended fruit compared to whole fruit and glucose concentration at 60 min tended to be lower ($p = 0.057$) in blended fruit compared to whole fruit. Unfortunately, the study was unable to measure insulin since this may have explained the lower glycemic response of the blended fruit as shown by Haber et al. (1977). The authors suggested that the reduced glycemic response in the blended fruit might be associated with the release of dietary fiber and components from ground blackberry seeds. Further that fruit smoothies without added sugar could be a healthy way of consuming the daily recommended amount of fruit.

Carotenoids in carrots are present in either crystalline form or bound to proteins within the chromoplasts. Hedrén, Diaz, and Svanberg (2002) examined the degree to which the physical structure of carrots needed disruption to allow carotenoids to be released from the chromoplasts and become bioaccessible as assessed by *in vitro* digestion. They showed that raw bitesize chunks, cooked bitesize chunks, raw pulped and pulped carrots cooked with 20 g rapeseed oil/100g carrot dry matter released 3, 6, 21 and 39% (P raw vs cooked < 0.05) of β-carotene respectively. The release of α-carotene was similar. The overall conclusion was that for carotenoid release, pulping was more effective than cooking, reflecting the need for cell wall disruption and the importance of the physical form of the food matrix.

Whilst the physical structure of a food's matrix can affect its impact and it is known that in dairy foods the calcium present can undergo saponification reactions in the digestive tract with food-derived fatty acids to produce inert soaps which may increase fat excretion and moderate blood lipid responses (see more below), there has been less study of any interaction between physical food form and the susceptibility for saponification to occur. This was examined by Lamothe et al. (2017) in a simulated gastrointestinal environment. They assessed the proportion of fat initially in various dairy food matrices that led to calcium soaps at the end of the digestion period. They used liquid (milk: three combinations of homogenization or not and heat treatment), semi-solid (yogurt: three types) and solid (cheese: made from four combinations of homogenized or not milk and pH) dairy matrices. Figure 1 shows the proportion of calcium soaps at the end of digestion and the calcium to lipid ratio of the various dairy foods.

Figure 1 shows that the liquid and semi-solid matrices gave rise to the lowest calcium soap formation and whilst there was some increase in soap formation in the milks and standard yogurt with higher calcium to lipid ratios, the gradient of the response was much less than seen for solid cheese matrices which also produced much more soap at the similar calcium to lipid ratios. The authors suggest this may be the result of the high calcium concentration from the cheese matrix particles in close proximity with the lipid droplets. Overall, calcium soap synthesis was much more efficient with the solid cheese matrices again indicating that the physical form of the matrix is important for its functionality. However, as the authors say, this work needed replication in human studies but is supported by the recent study of O'Connor et al. (2024). This randomized parallel human study compared the 6-week consumption of ~40 g of dairy fat as either unmelted Cheddar cheese, melted Cheddar cheese or a 'deconstructed' cheese (made up from butter, calcium caseinate and calcium carbonate) on changes in blood lipids, glucose and insulin concentrations. Comparisons of body weight, body mass index, body fat content and blood pressure were also made. There was no effect of dietary treatments on anthropometrics, blood pressure, fasted blood glucose and serum insulin but melted cheese increased total cholesterol concentration by 0.20 ± 0.15 mmol/L ($p = 0.008$) and triacylglycerol concentrations by 0.17 ± 0.08 mmol/L ($p = 0.016$) compared to unmelted cheese. No significant differences were seen for HDL-C, LDL-C and VLDL-C although the trend for LDL-C matched that of total cholesterol (Figure 2). These few examples illustrate the influence of the food matrix with respect to physical form on potential health impacts, some that are positive and some that are negative. Despite this improved knowledge, it remains unclear how this information can be incorporated into diet formulation and dietary guidelines that will account for matrix-related nutrient supply and effects on health.

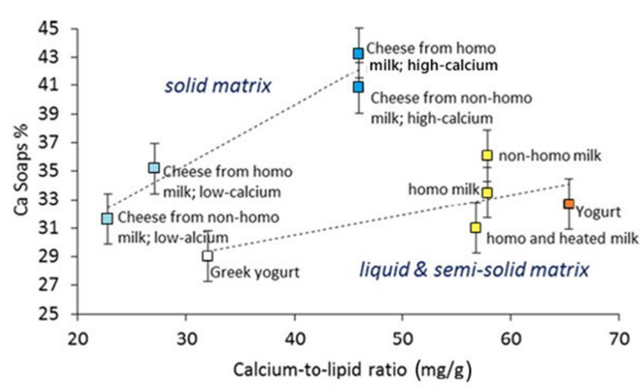


Figure 1. Relationship between the calcium soap % at the end of digestion and calcium to lipid ratio of the dairy matrices. H = homogenized, NH = not homogenized (from Lamothe et al. 2017).

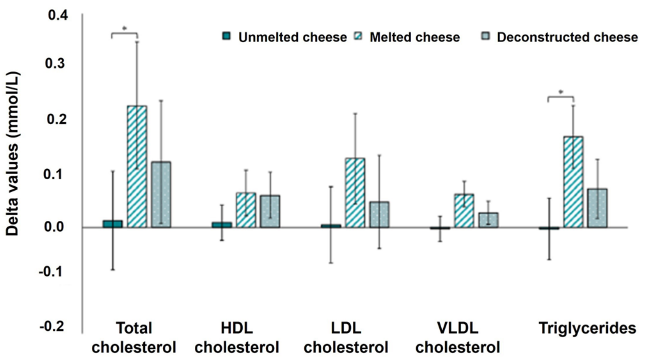


Figure 2. Effect of unmelted, melted and deconstructed cheese on changes in blood lipids (from O'Connor et al. 2024).

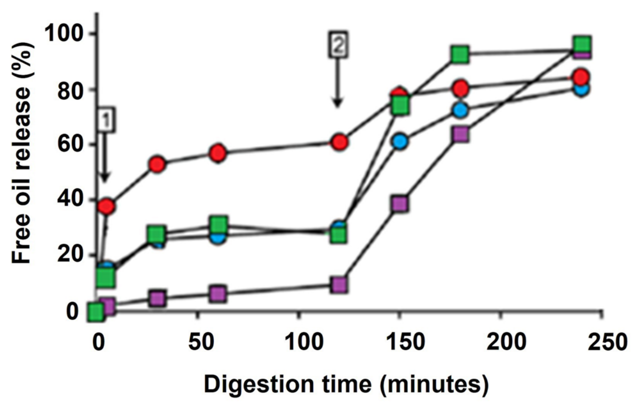


Figure 3. Rate of free oil release during digestion of aged Cheddar (red circle), mild Chedder (blue circle), light Cheddar (purple square) and Mozzarella (green square); 1, at start of gastric and 2, duodenal digestion (from Lamothe et al. 2012). © 2012. Lamothe, S., M.-M. Corbeil, S. L. Turgeon, and M. Britten All Rights Reserved. Reproduced with permission from Royal Society of Chemistry.

Effects of processing on nutrients and bioactive compounds

Lipids

There has been a large amount of research on the impact of dietary lipids particularly on cardiovascular diseases (CVD) with many controversies remaining. Much of this work has focused on fat type and particularly the perceived need to reduce intake of saturated fats to reduce the risk of CVD (e.g., reviews of Forouhi et al. 2018; Givens 2023). It is however known that the food matrix can influence the bioaccessibility of lipids in the food and subsequently the amount absorbed.

In plant sources of lipids, cell wall disruption is needed to enable lipid bioaccessibility for lipase activity in densely packed foods such as almonds. Grundy, Lapsley, and Ellis (2016) highlighted that the lipids in almonds are predominantly triaclyglycerols (TAG) and are stored within oil bodies in the almond kernels and it is predominantly the outer layer of cells of almond particles that fracture during mechanical processing or chewing in the mouth leading to much of the encapsulated lipid remaining intact and largely inaccessible to the lipases as shown by Grundy et al. (2015). A similar effect has been seen in relation to degradation of the cheese matrix during digestion being influenced by the physical characteristics of the cheese. Lamothe et al. (2012) compared the rate of free oil release (an index of matrix degradation) during gastric and duodenal digestion *in vitro* and rate of free fatty acid release during the duodenal phase of *in vitro* digestion of mild Cheddar, aged Cheddar, light Cheddar and Mozzarella cheese. During the gastric phase, the mean loss of free oil was three times greater for aged Cheddar cheese than the other cheeses (Figure 3). The authors suggested that this was likely due to the lower elasticity and cohesiveness of the aged Cheddar than the others which all showed similar matrix degradation characteristics in the gastric phase. The duodenal phase of digestion substantially increased the matrix degradation rate for all cheeses especially in the first 30 min (Figure 3).

During duodenal digestion the release of free fatty acids was highest for Mozzarella which agreed with its greater rate of matrix degradation and consequently increased the accessibility of lipase to the lipid. The overall conclusion was that the physical cheese matrix characteristics can substantially influence the ability of lipase to gain access to the lipid and thus affect the rate and extent of fatty acid release and absorption.

The study of Thorning et al. (2015) also examined the possibility that cheese ripening could lead to compositional changes to the cheese matrix which might influence metabolic responses after consumption. They used Cheddar cheese ripened for 4, 14 and 24 months and showed a positive relationship between ripening period and both amino acid and peptide concentrations, likely due the authors suggested, to the progressive proteolysis of casein. Using a pig model, they showed that whilst cheese ripening time had no significant effect on blood lipids apart from plasma non-esterified fatty acids which were significantly lower ($p = 0.01$) with the 14- and 24-month ripened cheese than the 4-month ripened. The 24-month ripened cheese also improved insulin sensitivity compared with the shorter ripening periods as indicated by lower serum insulin concentrations ($p = 0.008$) and reduced HOMA-IR ($p = 0.04$). There was no effect on plasma glucose. The increased concentrations of peptides and amino acids after an extensive ripening period are likely to have been accompanied by some changes in the cheese structure but whether this influenced the improvements in insulin function is not known.

Clearly there are several ways in which processing and the subsequent food matrix can influence lipid release and absorption but there remain uncertainties. As discussed in detail later in this overview, there is increasing evidence that the food source of saturated fat influences its impact on CVD with those from dairy foods having little or no effect yet those from red and particularly processed meat associated with increased CVD risk (e.g., Bechthold et al. 2019; Vogtschmidt et al. 2024). To what extent the processing and subsequent matrices of the two food groups influence this outcome is as yet unknown.

Carbohydrates

There is good evidence that dietary carbohydrates with a low glycemic index (GI) are beneficial for control of fasting blood glucose and particularly glycated hemoglobin in diabetics (Ojo et al. 2018). Foods with high GI rapidly increase blood glucose and insulin responses whilst those with a low GI have a slower impact on blood glucose levels and insulin response. Broadly, GI can be regarded as the relative rate of digestibility of the available carbohydrates of the food compared with glucose or a reference food. Despite this evidence there remains uncertainty about the impact of GI and glycemic load (GL) for reducing cardiometabolic diseases. Vega-López, Venn, and Slavin (2018) reported that results from studies over the last decade have not shown a clear clinical benefit for the use of GI, in part they suggest, since most data are from observational studies with limited dietary assessments not validated for assessment of GI and GL. Similarly, Jenkins and Willet (2024) reported that a recent WHO series of meta-analyses concluded that increases in dietary fiber and whole grains but not a reduction of GI or GL were needed for chronic disease reduction. With the increased rise in type 2 diabetes in many countries, approaches to enhance glycemic control are increasingly important both for prevention and treatment regimes. It is therefore vital that carbohydrates in diets are adequately characterized.

Except for dietary sugars, starch is the major contributor to carbohydrate intake in typical Western diets. Most of the starch is provided by cereals or foods they contribute to, notably bread. The GI of cereals and particularly their products is highly variable and dependent on intrinsic food matrix factors and extrinsic factors such as heat since cereal grains are usually thermally processed. The most important food matrix effect is the nature of the starchy endosperm including the proportion of RS type 1 starch which is isolated in intact endosperm cells which physically limit amylase access to the starch granules (Taylor, Naushad Emmambux, and Kruger 2015). Another matrix issue relates to the type of endosperm starch. Some cereals such as maize have genetically controlled two forms of endosperm, a dense outer vitreous layer and a less dense inner floury form. Correa et al. (2002) showed *in vitro* that the rate of starch digestion was negatively related to endosperm degree of vitreousness.

Figure 4. Time course increase (mean ± SEM) of postprandial blood glucose after consumption of 50 g carbohydrate in three forms. Difference from white bread: $^{*}p < 0.01$, $^{+}p < 0.05$ (from Jenkins et al. 1987). © 1987. Jenkins, D. J., M. J. Thorne, T. M. Wolever, A. L. Jenkins, A. V. Rao, and L. U. Thompson All Rights Reserved. Reproduced with permission from Elsevier.

Another important factor is the presence of prolamin proteins embedded into the endosperm. There is evidence that this protein-starch matrix limits expansion of the starch granule during cooking which would normally enhance the digestibility of the starch (Chandrashekar and Kirleis 1988). In a RCT, Jenkins et al. (1987) examined postprandial blood glucose increase following consumption of 50 g of carbohydrate as white bread, gluten-free white bread and gluten-free white bread plus added gluten to match the white bread. The glycemic responses are shown Figure 4. The moderation of blood glucose increase due to the gluten protein in the white bread endosperm matrix is clear as is the fact that simply adding gluten does not reproduce this effect.

This study is a good example of a food matrix effect involving the need to consider the combination of two macronutrients. Jenkins and Willet (2024) concluded that whilst dietary fiber and whole grain-containing foods are likely to provide health benefits, increased GI and GL will increase risk of chronic diseases. They recommended that all three characteristics, fiber/whole-grain, GI and GL, should be used in combination. This suggests it is important to understand the diet matrix rather than that of an individual food. Clearly more work is needed to further develop this concept.

Protein, protein quality

Protein quality assessment, the relationship to health, and implications for requirements are currently receiving much attention (Carbone et al. 2024). A report from the Agency for Healthcare Quality and Research has been released in advance of a study to reconsider protein requirements for North America by the National Academy of Medicine (Burstad et al. 2024). Expert panels will consider newer evidence on protein quality in revising requirements. Protein quality and functionality can be influenced by processing-induced changes in the food matrix. Dietary protein quality is primarily determined by the indispensable amino acid (IAA) content of a food as these amino acids cannot be synthesized and must be obtained from the diet. Traditionally, the protein quality of foods has been compared by their Protein Digestibility Corrected Amino Acid Score (PDCAAS). The PDCAAS is based on the profile and relative amounts of IAA in the food corrected for true fecal crude protein digestibility, relative to a profile of amino acid requirements with a value of 1 being the highest value. Table 1 shows PDCAAS scores for several foods, and because, the upper end is truncated, all complete proteins have a value of approximately 1. In 2013, the Food and Agriculture Organization of the United Nations recommended replacing PDCAAS with the Digestible Indispensable Amino Acid Score (DIAAS) to quantify dietary protein quality (Food and Agriculture Organization of the United

Table 1. PDCAAS and DIAAS scores for selected isolated proteins and foods for adolescents and adults (derived from Phillips 2017).

Food	PDCAAS	DIAAS	Limiting AA
Whole milk	1.00	1.43	Met + Cys
Milk protein concentrate	1.00	1.18	Met + Cys
Whey protein isolate	1.00	1.09	Val
Soy protein isolate	0.98	0.90	Met + Cys
Pea protein concentrate	0.89	0.82	Met + Cys
Tofu	0.70	0.98	Met + Cys
Cooked rice	0.62	0.59	Lys
Rice protein concentrate	0.58	0.82	Met + Cys
Chickpeas	0.52	0.67	Trp
Rice protein concentrate	0.42	0.37	Lys
Almonds	0.35	0.40	Lys
Corn-based cereal	0.08	0.01	Lys
Hydrolyzed collagen	0.00	0.00	Trp

Nations/World Health Organization 2013). The DIAAS is based on the relative digestible content of the IAAs and the amino acid requirement pattern with digestibility coefficients for each IAA based on the disappearance of amino acids from the gastrointestinal tract as measured at the end of the ileum (true ileal digestibility) in a pig model. In the case of lysine and processed food, digestibility is based on that of reactive lysine. This more demanding method offers advantages over PDCAAS including discriminating amongst high quality proteins (Wolfe et al. 2016). However, only a limited number of foods have DIAAS values. Examples of DIAAS scores are given in Table 1. In this scoring system, casein has a higher DIAAS value than egg or whey and corn has a lower value than wheat or rice. A new scoring system has been developed and validated, the Essential Amino Acid 9 (EAA-9) score (Forester et al. 2023). This system allows evaluation of each IAA individually based on amino acid requirements of an individual rather than on generalized protein patterns determined by analysis of previous scoring systems. Authors intend this system to be more consumer friendly. This system allows protein quality scores to be additive across multiple foods in a diet.

Processing can alter the quality of proteins from the generalized PDCAAS and DIAAS values. A good example is with cereals, an important source of dietary protein for humans. The limiting amino acid in children is lysine. Lysine contains a reactive side chain that can form unavailable lysine products with sugars during heating or storage through the Maillard reaction. Rutherfurd, Torbatinejad, and Mough (2006) evaluated 20 breakfast cereals for their digestible lysine content. The true ileal reactive lysine digestibility ranged from 53 to 108%. This three-fold difference was likely due to the different proportions of lysine in the cereal.

Heating can disrupt protein structures through denaturation, thereby altering the function of proteins and their digestibility. Protein can provide structure to more fragile structures like foamy desserts or gels to more substantive structures, like in gluten or meat.

Hydrated wheat gluten provides the viscoelastic matrix in baked products. In a dough, the high-molecular weight glutenins provide the elastic properties while gliadins act as a plasticizer. The formation of a viscoelastic protein network is crucial for gas retention during rising of the dough, and when baked, it provides the porous structure of bread and cakes (Aguilera 2019). The importance of gluten is obvious in gluten-free products. Gluten-free baked products lack the appearance, taste, aroma and texture of their all-wheat counterparts.

Cooking meat promotes the shrinkage and solubilization of the collagen matrix into gelatin (a process starting at around 60 °C) which tenderizes the meat, but heating also denatures myofibrillar proteins in meat fibers, leading to toughening and drip loss, that takes place between 52.5 and 60 °C (Zielbauer et al. 2016). Collagen crosslinks become stronger with aging of an animal which leads to progressive toughening of meat and increased flavor (Nishimura 2010).

Even a light heat treatment as occurs in pasteurization of milk alters the *in vitro* rates of protein hydrolysis and lipid release during digestion compared to raw milk (Ye et al., 2017). Using a sensitive nitrogen labeled milk in humans, Lacroix et al. (2008) found ultra-high temperature (UHT) pasteurization (140 °C for 5 s) increased protein digestibility and use compared to traditional pasteurization (72 °C for 20 s) or microfiltration. Differences in postprandial deamination losses were 25.9 +/− 3.3% of ingested nitrogen for the UHT group, 18.5 +/− 3.0% for the microfiltered group, and 18.6 +/− 3.7% for the traditional pasteurized group ($p \leq 0.0001$). When casein micelles partially disaggregate with heating, whey proteins such as β-lactoglobulin can be more rapidly hydrolyzed by pancreatic enzymes. The benefit of increased protein digestibility and utilization may be different for different individuals, i.e., obese or diabetic individuals may benefit from a lower nutrient-release rate whereas, elite athletes or older adults may benefit from an increased release rate.

Many other processes influence matrix effects on constituent functionality and digestibility. For example, digestibility of proteins and starch are improved due to their partial hydrolysis during sprouting of cereal grains (Lorenz and D'Appolonia 1980). Protein allergens in liquid matrices may be hydrolyzed so that individuals with intolerance can consume them safely.

Protein functionality: muscle protein synthesis

It is important to recognize that milk proteins have certain functionalities such as hypotensive effects which are not readily explained by traditional nutrition. An example is the hypotensive effects of milk proteins (e.g., Fekete et al. 2018) and the anabolic effect of whey protein in particular, for muscle protein synthesis. Aspects of the dairy matrix are involved in this.

One key feature of aging is the gradual loss of skeletal muscle mass and strength which if not moderated can lead to sarcopenia. Sarcopenia is associated with increased risk of bone fracture with potentially reduced mobility and self-dependence. Skeletal muscle also has a critical role in maintaining glucose homeostasis and is responsible for metabolic disposal of 70–90% glucose postprandially (Hulett, Scalzo, and Reusch 2022). Thus, reduced muscle mass, especially if associated with reduced ability to exercise and/or sarcopenic obesity, enhances insulin resistance and increases risk of type 2 diabetes (Hunter et al. 2019).

There has been much work on the relative anabolic effects of different protein types aimed at reducing muscle loss with an early review by Wall, Cermak, and Van Loon (2014). Broadly, the degree of muscle protein synthesis stimulated by dietary protein depends on its delivery of available amino acids and on the amino acid profile. Critically, it has been confirmed that the branched-chain amino acid leucine provides the key trigger for muscle protein synthesis (Zaromskyte et al. 2021). As a result, the role of whey protein, high in leucine, has been extensively studied in relation to effects on muscle protein synthesis. The role of leucine is complex with its effect being influenced by the food matrix providing it.

Burd et al. (2015) compared the protein digestion and absorption kinetics, post-prandial amino acid bioavailability and anabolic signaling effect on myofibrillar protein synthesis following consumption of skimmed milk vs minced beef. The cross-over design study involved young men immediately after completion of exercise. The skimmed milk and the beef both provided 30 g of protein and essentially matched leucine (milk 2.71, beef 2.48 g). Both treatments gave a rapid rise in plasma leucine concentration with the increase in the first 30 min being higher following milk than beef consumption, yet the beef led to a significantly higher ($p = 0.002$) peak leucine concentration (277 ± 12 µmol/L at 115 ± 8 mins) than the milk (231 ± 11 µmol/L at 235 ± 26 min). These results were reflected in a significantly higher ($p < 0.05$) myofibrillar protein synthetic rate in the first 2 h after milk than beef consumption (Figure 5) although the cumulative rates over 5 h were not significantly different despite the higher peak plasma leucine concentrations seen on the beef treatment. The results suggest that the milk matrix gave a more rapid release of leucine than that of the beef which was also accompanied by a significantly higher ($p \leq 0.05$) response in plasma insulin at 30 min after consumption. The higher insulin response from the milk may have contributed to the increase in myofibrillar protein synthetic rate in the first 30 min although Burd et al. (2015) suggest this is unlikely. They suggest that other factors in milk such as bioactive peptides and endogenous release of microRNAs may provide an anabolic stimulus to the muscles.

Other studies have compared the matrix effects of different milk products. Elliot et al. (2006) compared skimmed milk (237 g, 8.8 g protein), whole milk (237 g, 8 g protein) and skimmed milk (393 g,14.5g protein) on net muscle protein synthesis in young volunteers 60 min after resistance exercise. Total exchange of phenylamine and threonine across the legs were measured as indicators of net muscle protein synthesis since neither amino acid is metabolized in muscle.

As shown in Figure 6 threonine balance for the whole milk (8 g protein) was 312% greater than the skimmed milk (8.8 g protein) ($p \leq 0.05$) and 91% higher than for skimmed milk (14.5 g protein) although this difference was not significant. Results for phenylalanine were of the same direction but were not significant. Overall, the results suggest that providing protein in a whole milk matrix led to greater muscle protein synthesis than the same amount of protein in skimmed milk suggesting as Elliot et al. (2006) concluded that whole milk would be suitable for consumption during recovery from exercise.

Given that protein consumption increases the rate of muscle protein synthesis and the food matrix in which it is provided can alter the impact on muscle protein synthesis, Hermans et al. (2022) assessed the relative impact of providing protein in cheese compared to milk protein. The RCT with young males provided them with 30 g protein as cheese or a milk protein concentrate during recovery from exercise. The amino acid profile of the two protein sources was similar, e.g., the leucine concentration was 2.6 and 2.4 g per 30 g of protein for the milk protein concentrate and the cheese, respectively. Both sources of 30 g protein led to a significant increase in plasma amino acid concentration but the rise in that for leucine and total essential amino acids from the milk protein was quicker than for cheese leading to significantly higher concentrations at times from 30 to 120 min after consumption. Milk proteins also led to significant insulin response whereas the cheese did not. Despite these differences, muscle protein synthesis rates both at rest, and to a greater extent after exercise, increased on both treatments

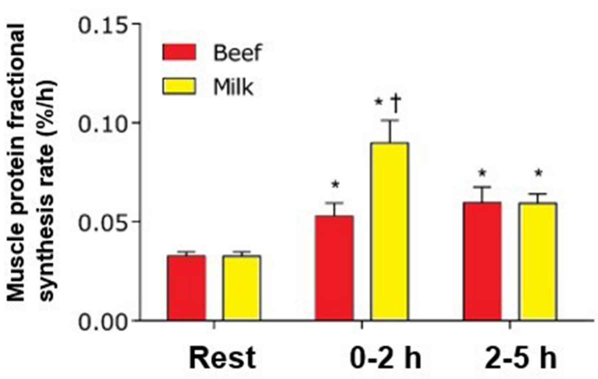


Figure 5. Mean (± SEM) myofibrillar protein synthesis rates before and after consumption of 30 g protein from skimmed milk or beef (from Burd et al. 2015). © 2015. Burd, N. A., S. H. Gorissen, S. van Vliet, T. Snijders, and L. J. C. van Loon. All Rights Reserved. Reproduced with permission from Elsevier.

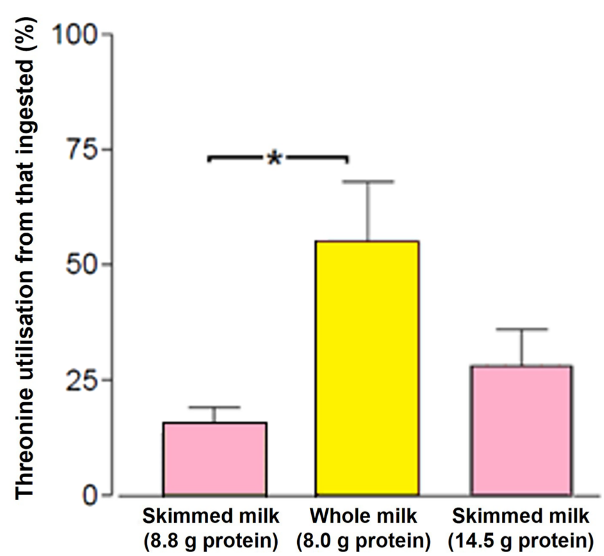


Figure 6. Ratio of threonine update across the legs relative to that ingested during recovery from exercise (from Elliot et al. 2006). © 2006. Elliot, T. A., M. G. Cree, A. P. Sanford, R. R. Wolfe, and K. D. Tipton. All Rights Reserved. Reproduced with permission from Wolters Kluwer Health, Inc.

by a similar amount with no significant difference between them. This seems to be an example of two contrasting matrices derived from the same primary food not leading to differences in outcome, at least in healthy young males. But as the authors conclude, it shows that protein-dense whole foods can be as effective as protein concentrates to support muscle protein synthesis.

As expert panels deliberate revising protein requirements, there will be much to consider. How will protein digestibility and functionality (e.g., muscle protein synthesis) factor into the recommendations? As the food matrix influences these properties, undoubtedly the panel will have a robust discussion of the role of the food matrix. Very likely requirements will be determined independent of the dietary source of protein with guidance for how dietary recommendations may be modified to meet biological requirements by considering the food supply. Much is known about food matrix effects on protein, but much is still to be learned.

Micronutrients

Essential micronutrients include vitamins and minerals. It has long been recognized that the food matrix influences bioaccessibility and bioavailability of micronutrients and a strong evidence base exists for many micronutrients. Bioaccessibility is the proportion of ingested nutrient that is available for absorption following digestive processes, whereas bioavailability is the proportion of the ingested nutrient that is absorbed and utilized through normal metabolic pathways. A micronutrient may be physically trapped within a dense food matrix making its release difficult through digestion, i.e., poorly bioaccessible. Or, it may be bound to an inhibitor that decreases absorption, i.e., poorly bioavailable. Alternatively, constituents may be present in the food which enhances absorption or utilization of a micronutrient. Iron bioavailability is much higher from animal sources than plant sources.

The most common inhibitors for mineral absorption are phytic acid, the storage form of phosphorus in seeds, and oxalic acid. The major staples in most diets which contribute the majority of energy intake are the cereal crops, i.e., wheat, corn, rice, barley, and oats, all seeds. The relative strength that minerals bind to phytic acid determines the relative inhibition of mineral absorption. Phytic acid binds more strongly to zinc than to calcium, and thus, the content of phytic acid is a stronger inhibitor of zinc absorption than calcium absorption. Processing that removes phytic acid (refining of cereals), hydrolyzes it (fermentation), or genetically reduces it improves bioavailability of bound minerals (Hambidge et al. 2005). Oxalic acid it the strongest inhibitor of calcium absorption because it forms the nearly insoluble salt, calcium oxalate. A bioavailability algorithm for calcium or prediction equation based on calcium, oxalate, and phytate content of foods was recently developed (Weaver et al. 2024). Prediction equations have also been proposed for zinc and iron (Armah et al. 2013; Hambidge et al. 2010; Miller, Krebs, and Hambidge 2007). The equation for zinc is mainly influenced by content of zinc and phytic acid in the food, whereas the equation for iron considered the iron status of the consumer. The poor iron absorption from plant sources may be a combination of lack of bioaccessibility from cellular components such as chloroplasts and mitochondria where iron is stored and the presence of inhibitors of iron absorption such as phytate. The relatively higher bioavailability from animal sources is associated with the absorption-enhancing effects of iron from heme and the absence of iron absorption inhibitors.

Bioavailability of micronutrients in the absence of barriers to bioaccessibility and inhibitors to absorption are typically much higher. Dairy products provide both bioaccessible and bioavailable micronutrients for this reason. Processing of milk into various dairy products does not influence calcium bioavailability regardless of physical form, lactose content, or protein aggregation as calcium absorption was not different from milk, yogurt, or cheese using intrinsically labeled milk and derived processed products with a stable calcium isotope (Nickel et al. 1996).

Unlike minerals, some vitamins need to be converted to an active form. For example, β-carotene, α-carotene and β-cryptoxanthin are dietary carotenoids that can be converted to vitamin A (retinol) through central cleavage by β-carotene monooxygenase. β-carotene is more abundant in the diet and is the most efficiently converted, but the food matrix has a great effect on bioavailability of β-carotene. β-carotene in chloroplasts of green leafy vegetables has much lower bioavailability than β-carotene from chromoplasts in fruits (Melse-Boonstra 2020). β-carotene in carrots where it exists in crystallized form is much less absorbed than when present in lipid droplets as occurs in papaya. Retinol activity equivalents (RAE) for β-carotene have been set at 12:1 (Institute of Medicine [IOM] 2001), though it can vary widely due to matrix effects (Melse-Boonstra 2020). Fiber can inhibit carotenoid absorption and fat content of the food or diet can greatly enhance carotenoid absorption (Brown et al. 2004; Goltz et al. 2012). Addition of fat generally improves bioavailability of fat-soluble vitamins (Gijsbers, Jie, and Vermeer 1996). As reported by Uwaezuoke (2017) there is an interaction between iron and high vitamin D potentially increasing iron status by suppressing hepcidin, a key hormone inhibitor of iron absorption. In addition, iron deficiency may exacerbate vitamin D deficiency by reducing the activity of the heme-containing 25- and 1α-hydroxylase enzymes needed for vitamin D activation reactions (Mogire et al. 2022). In addition, it is now also known that magnesium has a key role in both first and second stages of activation of vitamin D (Uwitonze and Razzaque 2018). There are thus key interdependencies of vitamins and minerals.

Processing can improve the bioavailability of bioactive constituents such as lycopene. In a clinical study of 36 healthy volunteers fed tomato sauce, tomato soup, or tomato juice ($n = 12$ per group) showed a greater accumulation of plasma lycopene and buccal mucosal cell lycopene which plateaued by two weeks in the highly processed tomato product (Allen et al. 2003). Compared to the two-week, lycopene-free run-in washout period, plasma lycopene increased by 192% when fed tomato sauce ($p < 0.0001$), 122% when fed the soup ($p < 0.0001$), and 92%, when fed the juice ($p < 0.0001$).

Although there is extensive literature on the matrix effects of particular micronutrients, the rapidly changing food supply will need new research. Extensive disruption and displacement of the matrix in traditional foods occurs as we move toward meat alternatives, plant-based food replacers, 3-D printing, UPF, and more.

Examples of food matrix complexity

Cow's milk and plant-based "milks"

Cow's milk is the top global dietary source of calcium, iodine, several B vitamins (including vitamin B_{12} not available from plant sources), and an array of essential amino acids reflecting its high-quality protein (Smith et al. 2021; Romulo 2022). Cow's milk is also an important source of vitamin A, potassium and magnesium. Cow's milk is considered minimally processed because the sold product appears as the source from the cow or other mammal. A generalized process is shown in Figure 7.

Plant-based milks are being selected as alternatives to cow's milk by individuals who have lactose maldigestion, allergies to milk proteins, or concern over environment and animal welfare. These milks are prepared by a generalized process as shown in Figure 8. As the figure shows, these processes use a great deal of water. Unlike cow's milk, the final products do not resemble the food source in appearance or nutrient composition. For example, see Table 2 which compares a 240 g serving of almond milk with 8 g of raw almonds, the amount contained in a serving of almond milk (USDA, 2023). Almond milk is fortified in calcium and potassium and has more sodium than the equivalent mass of almonds. The almond milk selected for this table was unsweetened, plain almond milk; some brands have added sugars.

In general, plant-based beverages begin with nuts or seeds such as almond, soybeans, oats, coconut, and rice which are milled, bleached, and ground, then combined with industrial ingredients and additives to stabilize the mix, colors and flavors, sugars to sweeten, and nutrients before further processing and packaging (Figure 8). These products are considered ultra-processed beverages unlike cow's milk (Drewnowski 2021).

The nutritional profile of five plant-based beverages from six brands were compared to cow's milk (Moore et al. 2024). Table 3, derived from that work, contrasts the nutrient profiles of these milks compared to cow's milk. Plant-based milks are much more variable in nutrient contribution than cow's milk demonstrating the lack of standardization for product processing, nutritional content, and quality compared to cow's milk with strict regulation. For example, obtaining calcium in the diet is a top expectation for people who choose to consume plant-based beverages rather than cow's milk. However, concentration of calcium can range from 0 to 1,253 mg/kg compared to an average of 1,049 mg/kg in cow's milk. Cow's milk is a major source of iodine. Plant-based milks are a poor source of iodine. Except for soy milk, plant-based milks are also lower in potassium and have a lower protein content compared to cow's milk. Furthermore, they cost consumers more than cow's milk. One 240 g serving of cow's milk may cost $0.24 compared to a serving of plant-based milks which range from $0.31 to $0.50.

Little is known about the effects of these changes in nutrient composition and matrices due to processing on health outcomes. Cases of severe nutritional deficiencies have been reported in infants with milk protein allergies fed nearly exclusively plant-based beverages as an alternative to infant formula (Le Louer et al. 2014; Katz et al. 2005) and in toddlers (Carvalho et al. 2001). Soymilk is the only plant-based beverage for which even calcium absorption has been measured (Zhao, Martin, and Weaver 2005). Calcium absorption was similar, especially if calcium was fortified as calcium carbonate rather than tricalcium phosphate. Soymilk has the most similar nutrient profile to milk. The lower protein content of the other plant-based milks compared to cow and soymilk can be expected to negatively affect calcium absorption (Kerstetter et al. 2005). From a single rat study, bone mineral content and density were higher in cow's milk and soymilk fed to growing rats than compared to growing rats fed almond milk (Cakebread et al. 2019). On the other hand, only cow's milk resulted in increased relative abundance of Bifidobacteriacea in that study (Cakebread et al. 2022).

Little is also known about the bioavailability of the nutrients in/or added to plant-based beverages despite its importance. The recent study of Muleya, Bailey, and Bailey (2024) compared the *in vitro* bioaccessible calcium from a 200 ml serving of various plant-based drinks and skimmed milk (Figure 9). None of the plant-based drinks nor many

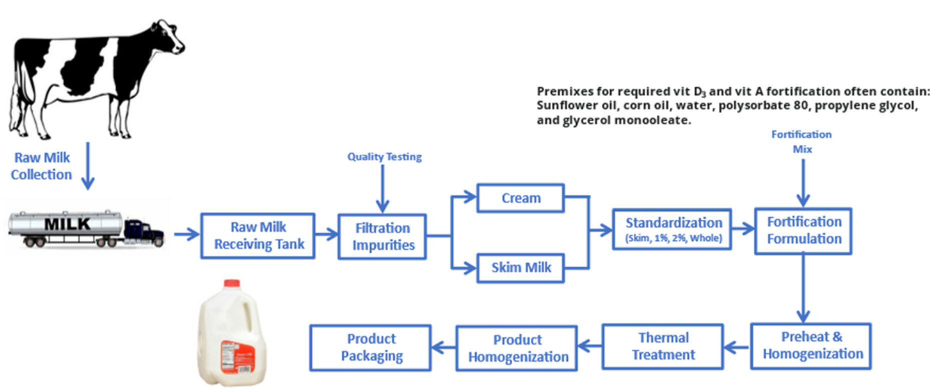


Figure 7. Generalized fluid milk processing (from Mario Ferruzzi, personal communication).

of the plant-based foods provided as much bioaccessible calcium as the cow's milk. This is likely to be a reflection of the casein protein micelles in milk which are supersaturated with calcium and deliver some 66% of total milk calcium which is known to be of high bioavailability (Toba et al. 1999). Casein micelles have a complex matrix and represent a matrix within the overall dairy matrix. However, it is important that alternative sources of calcium be tested for calcium absorption in humans beyond assessing only bioaccessibility for giving public health guidance.

Impact of foods co-consumed with olive products on bioavailability of key antioxidant polyphenols

It has been known for some time that consumption of Extra-virgin olive oil in the context of the Mediterranean diet is associated with reduced mortality and morbidity (European Union (EU)), 2012), predominantly due to the antioxidant functionality of several compounds present. The review of Servili et al. (2013) highlighted that the evidence was increasing that much of the healthiness of Extra-virgin olive oil was attributable to phenolic compounds present, which reduced peroxidation of blood lipids.

Although polyphenols are a very small fraction of olive oil, evidence suggests that they are of great importance in relation to its health benefits. This was highlighted in the early work of Carrasco-Pancorbo et al. (2005) which confirmed the importance of the hydroxyl groups as they enhance antioxidant activity with hydroxytyrosol (3, 4 dihydroxyphenyl ethanol) and related tyrosol (2, 4, hydroxyphenyl ethanol) being two of the key polyphenols. Hydroxytyrosol has been shown to inhibit oxidative damage resulting from reactive oxygen species which can be a substantial cause of endothelial dysfunction (Zrelli et al. 2011). A range of other health benefits of hydroxytyrosol and tyrosol have been reviewed more recently (Karković Marković et al. 2019).

Olive pomace and olive pomace wastewater are residues from olive oil production but contain considerably higher concentrations of hydroxytyrosol and tyrosol than in olive oil and recent work has focused on developing functional products from olive pomace extracts (Čepo et al. 2020). Clearly, the biochemical impact of hydroxytyrosol and tyrosol will only be expressed following intestinal absorption and there is already good evidence that the bioavailability of polyphenols in olive pulp extracts is relatively low with values for tyrosol reported as 16.2–16.8% based on amounts in Caco-2 cells as a percentage of the amount in the test meal before *in vitro* digestion (Malapert et al. 2018). Studies with rats to estimate the bioavailability of radio-labeled hydroxytyrosol and tyrosol when consumed in olive oil have reported values of 98–99% (Tuck et al. 2001) and this is supported by human studies (Bender, Strassmann, and Golz 2023). However, the high bioavailability values of hydroxytyrosol and tyrosol obtained for olive oil are not transferable to hydroxytyrosol and tyrosol in olive pomace extracts.

Bioavailability of polyphenols is dependent on their release from the matrix of foods present in the meal. This may especially be true for isolated bioactive constituents and reformulated food matrices. As a result of the lack of knowledge concerning the impact of food matrices, Čepo et al. (2020) carried out a series of studies which examined polyphenol-food type interactions to develop products that would deliver optimum doses of bioavailable hydroxytyrosol and tyrosol. This work used a combination of *in vitro* gastrointestinal digestion to measure bioaccessibility, and Caco-2 cells to assess the intestinal transepithelial

Table 2. Nutrient composition of one cup of almond milk and 8 g of almonds.

Trait	Almond Milk[1]	Almonds[2]
Serving (g)	240	8
Energy (kcal)	45.6	50
Total protein (g)	1.58	1.71
Fat (g)	3.74	4.09
Saturated fats (g)	0	0
Carbohydrates (g)	1.61	1.6
Fiber (g)	< 2	0.86
Minerals		
Ca (mg)	379	20.3
P (mg)	46	40.2
Mg (mg)	20	20.6
K (mg)	118	58.6
Na (mg)	142	< 1

[1]USDA, 2023 FoodData Central NDB # 100276.
[2]USDA 2023 FoodData Central NDB # 12061.

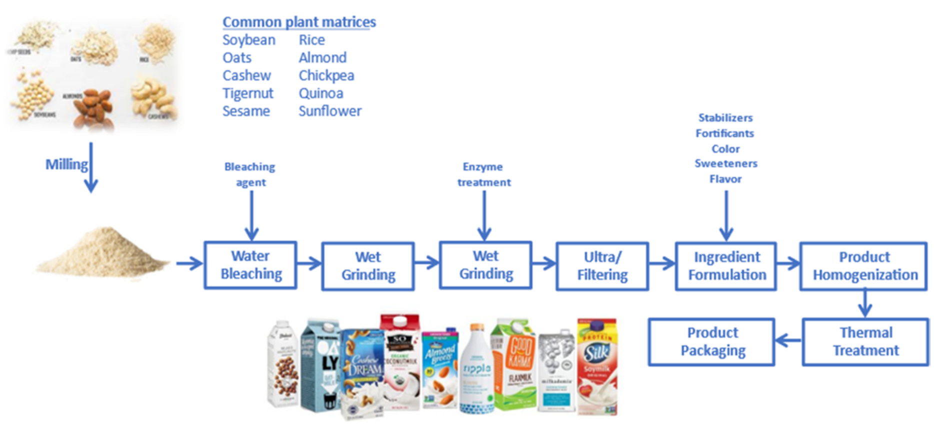


Figure 8. Generalized plant-based 'milk' processing (from Mario Ferruzzi, personal communication).

Table 3. The mean ± SD of gross composition and mineral content across brands of different plant-based beverages and cow's milk (derived from Moore et al. 2024).

Trait	Cow		Soy		Coconut		Oat		Almond	
n. samples (n. brands)	8 (4)		12 (6)		11 (6)		12 (6)		12 (6)	
Energy (kJ/100 mL)	276	8	167	19	156	82	209	34	216	156
Dry matter (%)	12.18	0.2	8.07	7.78	6.20	3.39	10.51	1.41	8.73	5.61
Ash (%)	0.72	0.02	0.46	0.09	0.19	0.04	0.18	0	0.15	0.07
Total protein (%)	3.39	0.10	3.35	0.48	0.23	0.09	0.70	0.26	0.99	0.85
Fat (%)	3.58	0.14	1.30	0.54	1.84	0.79	0.76	1.12	2.04	
Saturated fats (%)	2.53	0.04	1.78	1.14	1.83	0.60	0.12	0.08	0.23	0.13
Carbohydrates (%)	4.90	0.08	1.55	64	3.18	2.36	7.95	1.28	7.80	6.02
Total Sugar (%)	4.90	0.08	1.20	1.17	2.30	3.02	4.70	1.07	7.20	5.46
Lactose (%)	4.70	0.18	0.00	0	0.00	0	0.00	0	0.00	0
Glucose (%)	0.09	0.01	0.50	0.45	0.62	0.72	1.42	1.44	1.98	2.20
Fructose (%)	0.04	0.06	0.69	1.01	0.10	0.01	0.12	0.15	1.792	196
Salt (%)	0.11	0,0	0.09	0.04	0.10	17	0.09	0.03	0.07	0.03
Fiber (%)	0.00	0	0.98	1.10	0.32	10.32	0.40	0.40	0.41	0.35
Minerals										
I (µg/kg)	292	122	0	0	0	0	0	0	10	23
Ca (mg/kg)	1049	70	258	53	153	45	151	66	230	90
P (mg/kg)	926	75	499	117	54	19	155	44	147	68
Mg (mg/kg)	87	10	188	60	1672	3183	3452	4129	843	2712
K (mg/kg)	1396	81	1364	391	343	167	358	127	254	123
Na (mg/kg)	415	38	337	155	376	65	381	48	258	110
S (mg/kg)	241	30	201	47	0	0	14	17	0	23

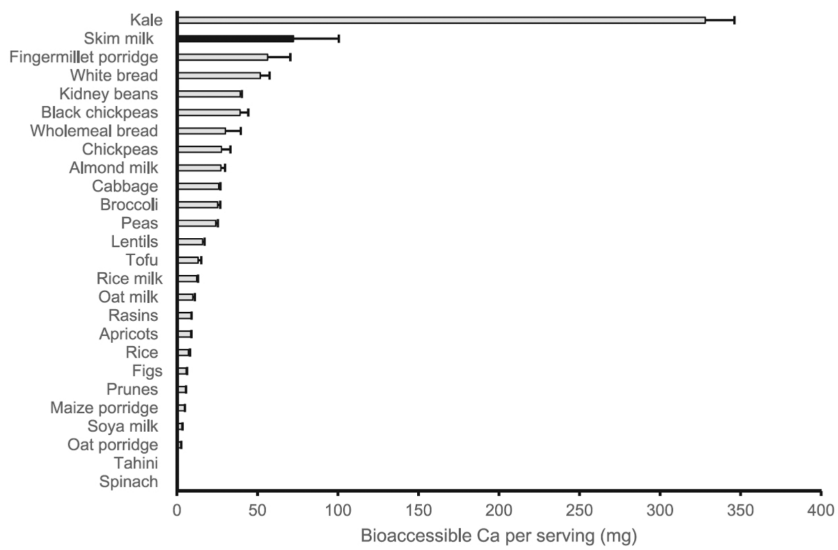


Figure 9. Ranking of the bioaccessible calcium per serving of 25 analyzed plant-based products compared with skim milk (from Muleya, Bailey, and Bailey 2024).

permeability of the two polyphenols. Dried olive pulp extract was co-digested with 19 different food products. The impact of the foods on bioaccessibility of hydroxytyrosol and tyrosol was expressed as relative bioaccessibility (RB) and was based on the outcome with and without the presence of the food products, i.e.,:

$$RB(\%)=\left(\frac{\text{bioaccessibility with food}(\%)}{\text{bioaccessibility without food}(\%)}\right)*100$$

Overall, it was shown that the bioaccessibility of hydroxytyrosol (78.4 to 103.9 mg/100g) and tyrosol (20.7 to 27.4 mg/100g) increased slightly, but significantly during gastrointestinal digestion, due to their liberation from a complex food matrix. It was also seen that the RB of hydroxytyrosol was significantly reduced during co-digestion of olive pulp extract with soya flakes, breakfast flakes, whole grain bread and apples whilst yogurt, milk formula, whole grain bread and apples particularly reduced RB for tyrosol (Figure 10). Interestingly, the RB of total phenols was particularly and significantly reduced by fresh low-fat cheese and soya flakes. Overall, protein-rich foods were particularly responsible for RB reductions with milk proteins in particular which supports earlier work showing that the antioxidant property of dietary phenolics are reduced due to their affinity for proteins, milk proteins in particular (Serafini et al. 2009). The food matrices examined did not produce any cytotoxic effects but may increase bilayer permeability as assessed using transepithelial transport of hydroxytyrosol and tyrosol.

Another study with 20 human subjects examined the bioavailability of hydroxytyrosol in a range of diverse and different food matrices (Alemán-Jiménez et al. 2021). The

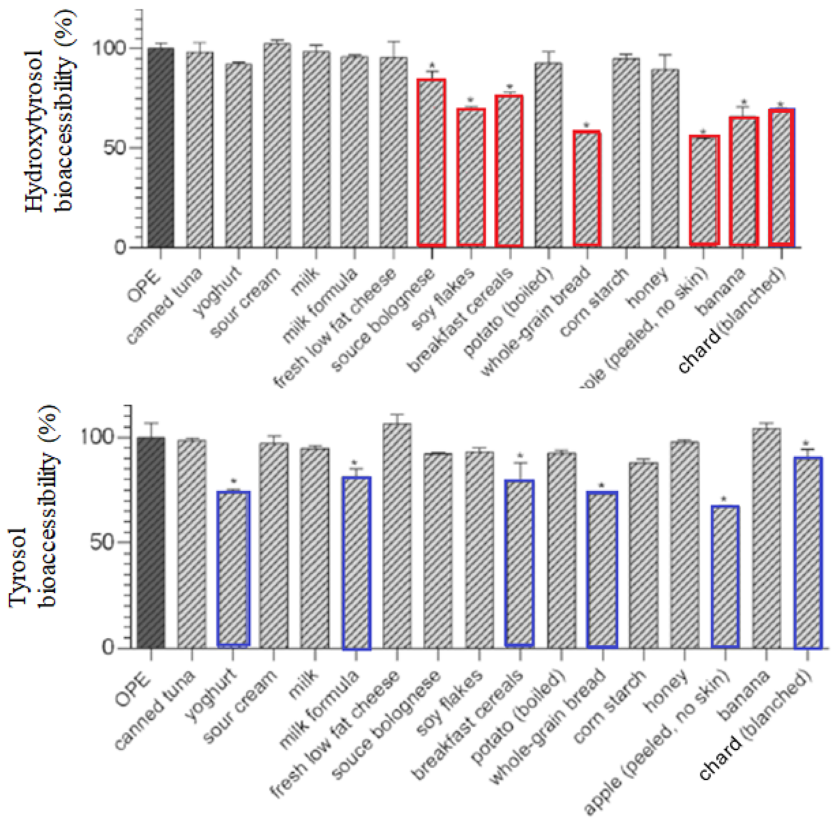


Figure 10. Effect of different food matrices on the relative bioaccessibility of tyrosol and hydroxytyrosol.(derived from Čepo et al. 2020).

subjects consumed 5 mg of hydroxytyrosol as a single dose within five fortified food matrices i.e., refined olive oil, flax oil, grapeseed oil, margarine and pineapple juice which were compared with extra virgin olive oil and a negative control of non-fortified olive oil. The relative bioavailability was assessed by measuring the concentration of hydroxytyrosol and its metabolites in peripheral blood and urine samples taken at intervals up to 240 min after consumption. Only the extra virgin olive oil and to a lower degree the fortified refined olive oil showed plasma concentrations of hydroxytyrosol higher than the control. Bioavailability assessed by urinary concentrations showed extra virgin olive oil, fortified refined olive, flax, and grapeseed oils to have significantly higher urinary concentrations than the other matrices with again the highest values being seen from the extra virgin oil.

Clearly the metabolic impact of hydroxytyrosol is highly dependent on the matrix it is within. Extra virgin olive oil was seen to be the best matrix, but it again highlights the challenge that is faced by the low bioavailability of polyphenols in olive pulp extracts.

Nutrient content versus whole foods and food patterns

The strongest evidence for the role of diet on health and disease prevention is for individual nutrients with evidence for foods and food patterns largely based on observational studies. Essential nutrient dietary intakes have been developed for many regions of the world. Evidence is reviewed to determine target intakes to prevent deficiencies, to reduce risk of chronic disease, and to avoid risk of harm due to excess. Until the recent development of methodologies to handle complex datasets to consider effects of interactions on multiple organs, researchers focused on studying single nutrients for a single outcome. Evidence is evaluated using a hierarchy of scientific approaches with randomized controlled trials providing causal links between diet and health outcomes and observational studies revealing associations for hypothesis development. Historically, the goal has been to guide consumers, health care professionals, and policy makers to prevent deficiencies of essential nutrients.

With the exception of dietary supplements that may provide isolated nutrients or bioactive compounds, consumers eat complex snacks, foods, and meals that contain an array of compounds that may interact to enhance or inhibit absorption or function. Expert panels that establish nutrient recommendations prioritize food over supplements first as a source of nutrients because the array of known and unknown constituents that can influence health of the consumer. Factors in foods including dose of constituents, chemical form of the compound and matrix, presence of absorption enhancers and inhibitors can influence bioavailability of nutrients.

Melse-Boonstra (2020) reviewed the importance of considering nutrient bioavailability in the context of the whole food. She emphasized that there is still much unknown. For example, fruits and vegetables are promoted for their health benefits, but studies have failed to identify these benefits in their isolated components. They contain pro-vitamin A carotenoids, vitamin C, folate, vitamin K-1, potassium, calcium, magnesium, iron, other trace elements, and many bioactive compounds including phenolics, carotenoids, glucosinolates, and fiber.

The quality of individual proteins was discussed earlier. Meat, casein, egg, and potato proteins have an average DIAAS above 100 and are classified as excellent (Herreman et al. 2020). Whey and soy proteins are classified as high-quality protein with an average DIAAS ≥75. In contrast, gelatin, rapeseed, lupin, canola, corn, hemp, fava bean, oat, pea, and rice proteins are classified in the no quality claim category with DIAAS <75. Yet, if consumed together, combinations of poor-quality proteins can provide complementary amino acids that raise the DIAAS values (Table 4); Herreman et al. 2020). Of course, small amounts of high-quality proteins can also complement poorer quality plant sources to improve the nutritional value.

Most nutrient interactions relate to effects of co-ingested foods or ingredients. For example, co-consumption of fat-soluble vitamins such as provided in salads and vegetables with oils or fat-containing foods such as egg can improve absorption of fat-soluble nutrients and bioactives such as vitamin E and carotenoids (Kim et al. 2015; Kim, Ferruzzi, and Campbell 2016; Goltz et al. 2013). Inhibitors to trace element absorption through forming insoluble salts in the gut have already been discussed. In contrast, some interactions occur that do not depend on co-ingestion. For example, 1,25-dihydroxycholecalciferol enhances active calcium absorption, but the benefit of vitamin D does not occur with calcium being consumed simultaneously. Vitamin D is converted to the active form when the calcium sensing receptors on the parathyroid gland, kidney, and bone marrow sense declining calcium levels and initiate the synthesis of the hydroxylating enzymes in the liver and kidney to convert the vitamin to its active form. This takes time and will influence calcium absorption from a later meal.

Manufacturers often formulate, enrich, or fortify foods to improve their nutrient content to make the nutrition label more attractive or as a strategy to address deficiencies. Examples include iodized salt, enrichment of refined flour, and fortification of cereals. Food engineering can take advantage of natural matrices to increase the nutrient contributions of ingredients and foods. An interesting example is the casein micelle. Casein micelles are combinations of all casein proteins αs1-, αs2-, β, and κ-casein and micellar calcium phosphate. The power of casein micelles to bind calcium in milk enables them to transport and deliver calcium and phosphate at concentrations significantly more than an order of magnitude exceeding the solubility of calcium phosphate. This is possible because most of the calcium and inorganic phosphate (Pi) in milk is in the form of micellar calcium phosphate held within the casein micelles. The calcium phosphate is encapsulated in the casein micelles in the form of small nanoclusters, with a typical diameter of 4–5 nm. A casein micelle, which contains several hundred calcium phosphate nanoclusters in addition to tens of thousands of casein molecules, can thus be considered a protein-based carrier for calcium phosphate. Casein micelles carry approximately two thirds of the total milk calcium, half the inorganic phosphate, one third of magnesium, and smaller proportions of citrate and the other small ions. The milk in the stomach is somewhat diluted and slightly acidified, as a result of which, some of the calcium phosphate that was present in the casein micelles will solubilize. Researchers are using re-assembled casein micelles (r-CM) to encapsulate micronutrients such as vitamins A and D or bioactives normally in low concentration in milk or that are polar to protect them from precipitation or degradation (Loewen, Chan, and Li-Chan 2018).

Table 4. Improved Digestible Indispensable amino acid Score (DIAAS) as a result of optimal plant protein combination (derived from Herriman, 2020).

Plant protein mixture	Max. DIAAS (≤100)	Ratio
Oat/lupin	76	7/93
Oat/lupin/soy	91	10/10/80
Oat/lupin/potato	100	10/20/60
Pea, wheat/potato	100	25/25/50
Soy/oat	92	90/10
Corn/potato	100	25/75
Wheat/potato	100	30/70

Coates et al. (2024) provides a vision of future dietary guidance that includes approaches using artificial intelligence (AI) and machine learning to analyze data from multi-omic and microbiome studies to inform dietary recommendations to population subgroups (i.e., precision nutrition) and to the individual level (i.e., personalized nutrition). These big data approaches are necessary to understand the complexity of dietary patterns over single nutrient effects on health.

Current controversies with a matrix implication

Good/bad saturated fat

One of the major controversies in recent times has been the apparent paradox that milk and dairy foods have a broadly neutral association with CVD risk (reviewed by Givens 2023). For many individuals, dairy products are the major dietary source of saturated fatty acids (SFA) which do stimulate increased concentrations of serum low density lipoprotein cholesterol (LDL-C). This has been the subject of several recent reviews (e.g., Astrup et al. 2021; Teicholz 2023; Givens 2023) and some key issues have emerged which to a certain extent explain this paradox.

These include the evidence which indicates that the food source and by implication different food matrices that supplies the SFA can influence the CVD risk. The early Multiethnic Study of Atherosclerosis (MESA) prospective study examining early, or subclinical atherosclerosis reported a 25% lower CVD risk (HR 0.75, 95%CI: 0.63-0.91) with the replacement of 2% energy intake (EI) of SFA from total meat by the same amount of SFA from total dairy (de Oliveira Otto et al. 2012). A similar finding was reported with data from the EPIC Netherlands cohort by Vissers et al. (2019) who showed that replacing 1% EI of dairy SFA by that from meat was associated with an increased CHD risk (HR 1.06, 95% CI: 1.02-1.10). Bechthold et al. (2019) undertook a systematic review and meta-analysis of 123 prospective studies on the associations between food groups and the risk of CHD, stroke and heart failure They reported that dairy food consumption was not associated with risk of

CHD (RR 0.99, 95% CI: 0.92-1.07), stroke (RR 0.96, 95% CI: 0.90-1.01) or heart failure (RR 1.00, 95% CI: 0.90-1.10) whilst red, and particularly processed meat, were significantly and positively associated with increased risk of all three disease outcomes. This is supported by a recent SFA replacement analysis which used data from the EPIC-Norfolk study (Vogtschmidt et al. 2024). This showed that replacement of SFA from all meat by SFA from dairy was associated with a less CVD (HR 0.89, 95% CI: 0.82-0.96) and coronary artery disease (HR 0.88, 95% CI: 0.80-0.96). The impact of replacing SFA from processed meat by those from milk or cheese also showed a reduction in CVD (milk: HR 0.84, 95% CI: 0.74-0.94; cheese: HR 0.77, 95% CI: 0.68-0.88). These findings could have substantial implications for public dietary guidance although they do need confirmation from appropriate RCTs.

Various proposals for the reasons why dairy and meat display opposite risk for CVD and related conditions have been made. Mozaffarian (2016) has suggested that the increased risk associated with red and processed meat may be related to the presence of pro-inflammatory and/or pro-oxidative compounds initiated by nitrosamines, heme iron, SFA and high sodium especially in processed meat. Others suggest that the dairy matrix may have beneficial characteristics which are not fully explained by single components in the foods but may involve interactions within the dairy matrix (Thorning et al. 2017).

It has also been shown that responses in blood lipids can vary in response to intake of different dairy foods. The 4-week cross-over RCT of Brassard et al. (2017) showed that whilst consuming diets providing ~12.4% EI from SFA supplied by butter or cheese produced similar responses in HDL-C, but LDL-C was significantly lower (-3.3%, $p<0.05$) after the cheese than the after the butter diet. This study is supported by a range of studies and reviews on the dairy food matrix comparing blood lipid responses to SFA from cheese vs. butter (e.g., Hjerpsted, Leedo, and Tholstrup 2011; Feeney et al. 2018; Feeney and McKinley 2020) which show the same differential effects. Aspects of this have been discussed earlier concerning the higher calcium concentration in cheese than butter and the related calcium saponification reactions linked to more solid food matrix types such as hard cheese which leads to increased fecal fat excretion. It is also noteworthy that Lorenzen and Astrup (2011) showed that the cholesterol lowering effect was greater than could be explained by increased fecal fat excretion. They did however show that there was an interaction between calcium and bile acids such that increased fecal bile acid excretion occurred and was associated with less bile acid recycling through entero-hepatic circulation. This may result in enhanced uptake of circulating cholesterol by the liver for synthesis of bile acids resulting in reduced LDL-C concentration in the blood.

Overall, there is increasing doubt about the validity of the traditional diet-heart hypothesis which positively links increased SFA consumption with increased serum cholesterol concentration and subsequent increased risk of CVD. Whilst serum cholesterol concentrations generally do increase following SFA intake, this is without a consistent increase in CVD risk, despite LDL being a known causal issue in atherosclerotic CVD. Emerging evidence to explain this apparent paradox is very relevant to dairy foods. These include the possible compensating role of SFA-stimulated HDL-C, hypotensive effects of milk and food matrix effects which moderate serum LDL-C concentrations. It is now known that SFA generally lead to production of the less atherogenic large buoyant LDL particles rather than consistently atherogenic small dense LDL particles (Froyen 2021) although it is not known if this is a feature unique to SFA in dairy fat.

Ultra-processed foods

In recent years, health concerns over industrial-processed foods or ingredients have led to policy recommendations in some countries (several Latin American countries, Israel, and Malaysia, among others), research activity, and great interest by the public. A scientific statement by the American Society of Nutrition over a decade ago warned to be careful when considering limiting processed foods as they provide large contributions of essential nutrients in the American diet, i.e., 57% of fiber, 48% of calcium, 43% of potassium, 34% of vitamin D, 64% of iron, 65% of folate, and 46% vitamin B1 (Weaver et al. 2014). An update of concern over limiting UPF from the diet was recently published (Trumbo et al. 2024). UPF can include nutrient dense and healthy choice foods such as yogurt, olive oil, bread, and ready-to-eat cereal.

The scientific statement discussed above (Weaver et al. 2014) distinguished between processing as steps in transforming food into forms consumed and formulation or recipes which determine the nutrient composition. A point of confusion is that there is no universally accepted definition of UPF. Many classification systems exist and often they use a mixture of extent of processing and formulations. The classification system that has received the most attention is the Nova system (Monteiro et al. 2018). The Nova system defines four levels of processing: minimally processed foods, processed culinary ingredients, processed foods, and UPF. The latter are defined as foods which contain "substances never or rarely used in kitchens, or classes of additives whose function is to make the final product palatable or more appealing". Classification systems based on processing have no scientific rationale and without clearly defined categories, are subject to highly variable assignments even by nutrition experts (Gibney 2023). Furthermore, the evidence does not show a relationship between UPF consumption and dietary patterns that are low in micronutrients (Gibney et al. 2017). The United Kingdom Scientific Advisory Committee on Nutrition (SACN) recently concluded that food classification systems based on processing level are inconsistent or lack clarity on the various food components (SACN, 2023), and the 2025–2030 Dietary Guidelines for Americans (DGA) considered for the first time a systematic literature review on the question: "What is the relationship between consumption of dietary patterns with varying amounts of UPF and growth, body composition, and risk of obesity?" They found limited evidence and could not justify including recommendations around UPF (Dietary Guidelines for Americans Advisory Committee, 2023).

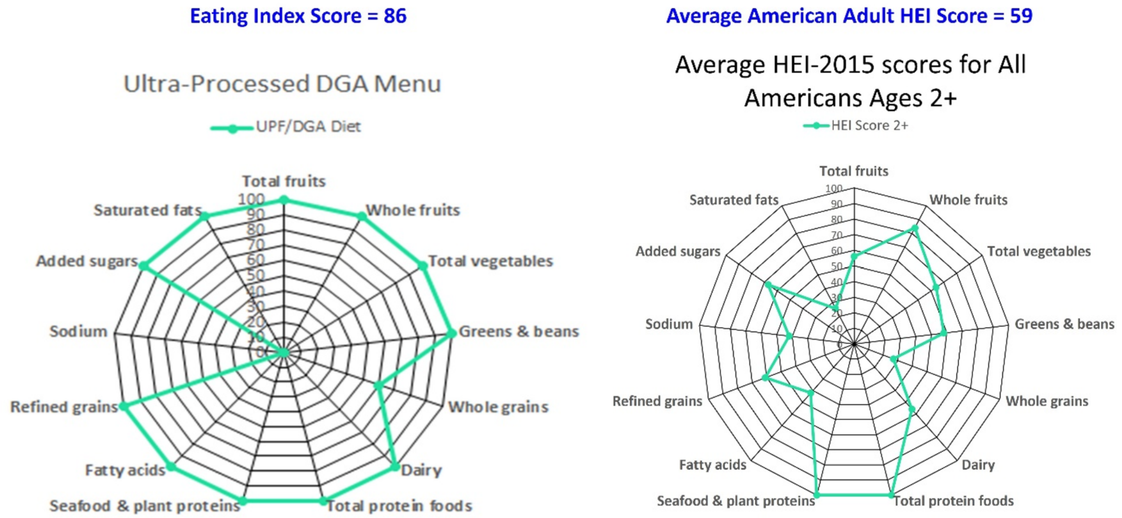


Figure 11. Diet quality scores for ultra-processed DGA menu and an average American Healthy Eating Index 2015. (Derived from Hess et al. 2023).

Historically, the DGA have been based on dietary patterns associated with health from evidence and nutrient density via the Healthy Eating Index. The purpose and extent of food processing does not determine a food's nutrient density and is not a validated tool to measure diet quality.

Food processing is critical to sustain a safe, affordable, and nutritious food supply. The extent of processing *per se* is not what determines the nutrient content of foods. Hess et al. (2023) used the Nova classification system to select UPF to determine if they could meet the DGA with exclusively UPF. Figure 11 shows that they could achieve a HEI diet score of 86 with UPF compared to the average American HEI score of 59. The only food category that could not be achieved with UPF was whole grains as most breads and cereals are classified as UPF by the NOVA system.

Processing can alter the food matrix as illustrated with the example above comparing cow's milk and plant-based beverages or by transforming milk into cheese or yogurt as will be described in subsequent articles. There are numerous examples of both positive and negative consequences to health attributed to processing described here and elsewhere (Trumbo et al. 2024). The availability of a safe, available, sustainable, and nutritious food supply remains a priority. To provide the best food supply for health will be guided more by the formula or recipe than the extent of processing. To be mindful of providing a healthful food supply should be a guiding principle of all involved.

Conclusions, research gaps and opportunities

Research on food matrix effects on diet and health has increased our understanding that the health impacts of a food or diet are more than their composition of nutrients. Processing of foods can alter the food matrix and health effects in both positive and negative ways. This knowledge can guide product development and meal planning. The dairy matrix is the most studied. Our understanding of the effects of even the dairy matrix is incomplete and the field is almost wide open for any other food. The most urgent need for safety is to understand staple food replacements in order to avoid disastrous consequences such as those discussed on replacing cow's milk with plant-based beverages during growth. Recent achievements in food manufacturing that give us plant-based meat alternatives, 3-D printed foods, and UPF require research to understand the nutritional impact of drastic changes in the traditional food matrix. To expect consumers to understand ongoing research about the food matrix and how to translate it into what they should eat is unfeasible. Giving advice on whole foods to consume rather than their isolated ingredients is more achievable. Recommending food patterns that include dairy, fruits, and vegetables or to include at least small amounts of high-quality protein in a plant forward diet is easily translatable and actionable rather than giving specific advice on milk fat globule membrane, complementary amino acids, etc. Nevertheless, for those choosing restricted diets, more education and thoughtful choices are warranted.

Disclosure statement

CMW has an active grant with the National Dairy Council on "Racial and ethnic differences in calcium absorption and mineral metabolism in response to dietary salt" and has received travel expenses and honoraria in connection with lectures and meetings from the National Dairy Council, the Global Dairy Platform, and the International Dairy Federation. DIG has received travel expenses and honoraria in connection with lectures and meetings from the Dairy Council (now Dairy UK), Dutch Dairy Association, European Milk Forum, and the International Dairy Federation. He has also been a consultant to BioCC OÜ the Estonian Bio-Competence Center of Healthy Dairy Products, to the Dairy Council (now Dairy UK) on fats in dairy products and cardiometabolic diseases and to the School and Nursery Milk Alliance on research evidence on the role of milk in the diets of infants and children.

Author contributions statement

CMW and DIG designed and conceptualized the narrative review; conducted literature searches, interpreted published findings; and drafted and revised the final manuscript. Both authors agree to be accountable for all aspects of the work.

Funding

This work was supported by the Dairy Research Consortium.

ORCID

Connie M. Weaver http://orcid.org/0000-0002-5450-9609
D. Ian Givens http://orcid.org/0000-0002-6754-6935

References

Aguilera, J. M. 2019. The food matrix: Implications in processing, nutrition and health. *Critical Reviews in Food Science and Nutrition* 59 (22):3612–29. doi: 10.1080/10408398.2018.1502743.

Alemán-Jiménez, C., R. Domínguez-Perles, S. Medina, I. Prgomet, I. López-González, A. Simonelli-Muñoz, M. Campillo-Cano, D. Auñón, F. Ferreres, and Á. Gil-Izquierdo. 2021. Pharmacokinetics and bioavailability of hydroxytyrosol are dependent on the food matrix in humans. *European Journal of Nutrition* 60 (2):905–15. doi: 10.1007/s00394-020-02295-0.

Allen, C. M., S. J. Schwartz, N. E. Craft, E. L. Giovannucci, V. L. de Groff, and S. K. Clinton. 2003. Changes in plasma and oral mucosal lycopene isomer concentrations in healthy adults consuming standard servings of processed tomato products. *Nutrition and Cancer* 47 (1):48–56. doi: 10.1207/s15327914nc4701_6.

Armah, S. M., A. Carriquiry, D. Sullivan, J. D. Cook, and M. B. Reddy. 2013. A complete diet-based algorithm for predicting nonheme iron absorption in adults. *The Journal of Nutrition* 143 (7):1136–40. doi: 10.3945/jn.112.169904.

Astrup, A., N. Teicholz, F. Magkos, D. M. Bier, J. T. Brenna, J. C. King, A. Mente, J. M. Ordovas, J. S. Volek, S. Yusuf, et al. 2021. Dietary saturated fats and health: Are the U.S. guidelines evidence-based? *Nutrients* 13 (10):3305. doi: 10.3390/nu13103305.

Bechthold, A., H. Boeing, C. Schwedhelm, G. Hoffman, S. Knüppel, K. Iqbal, S. De Henauw, N. Michels, B. Devleesschauwer, S. Schlesinger, et al. 2019. Food groups and risk of coronary heart disease, stroke and heart failure: A systematic review and dose-response meta-analysis of prospective studies. *Critical Reviews in Food Science and Nutrition* 59 (7):1071–90. doi: 10.1080/10408398.2017.1392288.

Bender, C., S. Strassmann, and C. Golz. 2023. Oral bioavailability and metabolism of hydroxytyrosol from food supplements. *Nutrients* 15 (2):325. doi: 10.3390/nu15020325.

Brassard, D., M. Tessier-Grenier, J. Allaire, E. Rajendiran, Y. She, V. Ramprasath, I. Gigleux, D. Talbot, E. Levy, E. Levy, et al. 2017. Comparison of the impact of SFAs from cheese and butter on cardiometabolic risk factors: A randomized controlled trial. *The American Journal of Clinical Nutrition* 105 (4):800–9. doi: 10.3945/ajcn.116.150300.

Brown, M. J., M. G. Ferruzzi, M. L. Nguyen, D. A. Cooper, A. L. Eldridge, S. J. Schwartz, and W. S. White. 2004. Carotenoid bioavailability is higher from salads ingested with full-fat than with fat-reduced salad dressings as measured with electrochemical detection. *The American Journal of Clinical Nutrition* 80 (2):396–403. doi: 10.1093/ajcn/80.2.396.

Burd, N. A., S. H. Gorissen, S. van Vliet, T. Snijders, and L. J. C. van Loon. 2015. Differences in postprandial protein handling after beef compared with milk ingestion during postexercise recovery: A randomized controlled trial. *The American Journal of Clinical Nutrition* 102 (4):828–36. doi: 10.3945/ajcn.114.103184.

Burstad, K., A. Erickson, E. Gholizadeh, H. Namigga, A. M. Claussen, T. Lamina, J. Slavin, L. Teigen, K. Hill Gallant, J. Stang, et al. 2024. Evaluation of dietary protein and amino acid requirements: A systematic review. Systematic Review. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 75Q80120D00008.) AHRQ Publication No. 24(25)-EHC030. Rockville, MD: Agency for Healthcare Research and Quality. doi: 10.23970/AHRQEPCSRPROTEINAMINO.

Cakebread, J. A., O. A. M. Wallace, H. Henderson, R. Jauregui, W. Young, and A. Hodgkinson. 2022. The impacts of bovine milk, soy beverage, or almond beverage on the growing rate microbiome. *PeerJ.* 10:e13415. doi: 10.7717/peerj.13415.

Cakebread, J. A., O. A. M. Wallace, M. C. Kruger, M. H. Vickers, and A. J. Hodgkinson. 2019. Supplementation with bovine milk or soy beverages recovers bone mineralization in young growing rats fed an insufficient diet, in contrast to an almond beverage. *Current Developments in Nutrition* 3 (11):nzz115. doi: 10.1093/cdn/nzz115.

Carbone, J. W., S. M. Phillips, C. M. Weaver, J. M. Hughes, and S. M. Pasiakos. 2024. Exploring opportunities to better characterize the effects of dietary protein on health across the lifespan. *Advances in Nutrition (Bethesda, MD)* 16 (1):100347. Epub ahead of print. PMID: 39608572. doi: 10.1016/j.advnut.2024.100347.

Carrasco-Pancorbo, A., L. Cerretani, A. Bendini, A. Segura-Carretero, M. del Carlo, T. Gallina-Toschi, G. Lercker, D. Compagnone, and A. Fernández-Gutiérrez. 2005. Evaluation of the antioxidant capacity of individual phenolic compounds in virgin olive oil. *Journal of Agricultural and Food Chemistry* 53 (23):8918–25. doi: 10.1021/jf0515680.

Carvalho, N. F., R. D. Kenney, P. H. Carrington, and D. E. Hall. 2001. Severe nutritional deficiencies in toddlers resulting from health food milk alternatives. *Pediatrics* 107 (4):E46–e46. doi: 10.1542/peds.107.4.e46.

Čepo, D. V., K. Radić, P. Turčić, D. Anić, B. Komar, and M. Šalov. 2020. Food (Matrix) effects on bioaccessibility and intestinal permeability of major olive antioxidants. *Foods (Basel, Switzerland)* 9 (12):1831. doi: 10.3390/foods9121831.

Chandrashekar, A., and A. W. Kirleis. 1988. Influence of protein on starch gelatinization in sorghum. *Cereal Chemistry* 65:457–62.

Coates, P. M., R. L. Bailey, J. B. Blumberg, A. El-Sohemy, Z. E. Floyd, J. Z. Goldenberg, A. Gould Shunney, H. D. Holscher, Y. Nkrumah-Elie, D. Rai, et al. 2024. The evolution of science and regulation of dietary supplements: Past, present, and future. *The Journal of Nutrition* 154 (8):2335–45. doi: 10.1016/j.tjnut.2024.06.017.

Correa, C. E. S., R. D. Shaver, M. M. Pereira, J. D. Lauer, and K. Kohn. 2002. Relationship between corn vitreousness and ruminal in situ starch degradability. *Journal of Dairy Science* 85 (11):3008–12. doi: 10.3168/jds.S0022-0302(02)74386-5.

Crummett, L. T., and R. J. Grosso. 2022. Postprandial glycemic response to whole fruit versus blended fruit in healthy, young adults. *Nutrients* 14 (21):4565. doi: 10.3390/nu14214565.

de Oliveira Otto, M. C., D. Mozaffarian, D. Kromhout, A. G. Bertoni, C. T. Sibley, D. R. Jacobs, Jr., and J. A. Nettleton. 2012. Dietary intake of saturated fat by food source and incident cardiovascular disease: The Multi-Ethnic Study of Atherosclerosis. *The American Journal of Clinical Nutrition* 96 (2):397–404. doi: 10.3945/ajcn.112.037770.

Dietary Guidelines for Americans Advisory Committee. 2023. Processed-Foods-and-Health.pdf (Accessed 16 July 2023) Dietary Guidelines for Americans. Work under way. Dietary Guidelines for Americans Advisory Committee: Meeting 2. Available at: https://www.dietaryguidelines.gov/sites/default/files/2023-08/DGAC_Mtg_2_Summary_05.10.2023_508c_Secured.pdf

Drewnowski, A. 2021. Perspective: Identifying ultra-processed plant-based milk alternatives in the USDA branded food products database. *Advances in Nutrition (Bethesda, MD)* 12 (6):2068–75. doi: 10.1093/advances/nmab089.

Elliot, T. A., M. G. Cree, A. P. Sanford, R. R. Wolfe, and K. D. Tipton. 2006. Milk ingestion stimulates net muscle protein synthesis following resistance exercise. *Medicine and Science in Sports and Exercise* 38 (4):667–74. doi: 10.1249/01.mss.0000210190.64458.25.

European Union (EU). 2012. Commission Regulation (EU) No 432/2012 of 16 May 2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health. *Offical Journal of the European Union* L136:1–40.

Feeney, E. L., and M. C. McKinley. 2020. The dairy food matrix: What it is and what it does. In *Milk and dairy foods: Their functionality in human health and disease*, 205–25. Cambridge, MA: Academic Press/Elsevier.

Feeney, E. L., R. Barron, V. Dible, Z. Hamilton, Y. Power, L. Tanner, C. Flynn, P. Bouchier, T. Beresford, N. Noronha, et al. 2018. Dairy matrix effects: Response to consumption of dairy fat differs when eaten within the cheese matrix-a randomized controlled trial. *The American Journal of Clinical Nutrition* 108 (4):667–74. doi: 10.1093/ajcn/nqy146.

Fekete, Á. A., C. Giromini, Y. Chatzidiakou, D. I. Givens, and J. A. Lovegrove. 2018. Whey protein lowers systolic blood pressure and Ca-caseinate reduces serum TAG after a high-fat meal in mildly hypertensive adults. *Scientific Reports* 8 (1):5026. doi: 10.1038/s41598-018-23333-2.

Food and Agriculture Organization of the United Nations/World Health Organization. 2013. *Dietary protein quality evaluation in human nutrition: Report of an FAO expert consultation*. Rome, Italy: FAO Food and Nutrition. Paper 92.

Forester, S. M., E. M. Jennings-Dobbs, S. A. Sathar, and D. K. Layman. 2023. Perspective: Developing a nutrient-based framework for protein quality. *The Journal of Nutrition* 153 (8):2137–46. doi: 10.1016/j.tjnut.2023.06.004.

Forouhi, N. G., R. M. Krauss, G. Taubes, and W. Willett. 2018. Dietary fat and cardiometabolic health: Evidence, controversies, and consensus for guidance. *BMJ (Clinical Research ed.)* 361:k2139. doi: 10.1136/bmj.k2139.

Froyen, E. 2021. The effects of fat consumption on low density lipoprotein particle size in healthy individuals: A narrative review. *Lipids in Health and Disease* 20 (1):86. doi: 10.1186/s12944-021-01501-0.

Gibney, M. J. 2023. Ultra-processed foods in public health nutrition: The unanswered questions. *British Journal of Nutrition* 129 (12):2191–4. doi: 10.1017/S0007114522002793.

Gibney, M. J., C. G. Forde, D. Mullally, and E. R. Gibney. 2017. Ultra-processed foods in human health: A critical appraisal. *The American Journal of Clinical Nutrition* 106 (3):717–24. Erratum in: American Journal of Clinical Nutrition. 107:482-483. doi: 10.3945/ajcn.117.160440.

Gijsbers, B. L. M. G., K.-S. G. Jie, and C. Vermeer. 1996. Effect of food composition on vitamin K absorption in human volunteers. *The British Journal of Nutrition* 76 (2):223–9. doi: 10.1079/bjn19960027.

Givens, D. I. 2023. Dairy foods and cardiometabolic diseases: An update and a reassessment of the impact of saturated fatty acids. *Proceedings of the Nutrition Society* 82 (3):329–45. doi: 10.1017/S0029665123000083.

Goltz, S. R., T. N. Sapper, M. L. Failla, W. W. Campbell, and M. G. Ferruzzi. 2013. Carotenoid bioavailability from raw vegetables and a moderate amount of oil in human subjects is greatest when the majority of daily vegetables are consumed at one meal. *Nutrition Research (New York, NY)* 33 (5):358–66. doi: 10.1016/j.nutres.2013.02.010.

Goltz, S. R., W. W. Campbell, C. Chitchumroonchokchai, M. L. Failla, and M. G. Ferruzzi. 2012. Meal triacylglycerol profile modulates postprandial absorption of carotenoids in humans. *Molecular Nutrition & Food Research* 56 (6):866–77. doi: 10.1002/mnfr.201100687.

Grundy, M. M.-L., K. Lapsley, and P. R. Ellis. 2016. A review of the impact of processing on nutrient bioaccessibility and digestion of almonds. *International Journal of Food Science & Technology* 51 (9):1937–46. doi: 10.1111/ijfs.13192.

Grundy, M. M.-L., P. J. Wilde, P. J. Butterworth, R. Gray, and P. R. Ellis. 2015. Impact of cell wall encapsulation of almonds on in vitro duodenal lipolysis. *Food Chemistry* 185:405–12. doi: 10.1016/j.foodchem.2015.04.013.

Haber, G. B., K. W. Heaton, D. Murphy, and L. F. Burroughs. 1977. Depletion and disruption of dietary fibre: Effects on satiety, plasma glucose, and serum insulin. *Lancet (London, England)* 2 (8040):679–82. doi: 10.1016/s0140-6736(77)90494-9.

Hambidge, K. M., L. V. Miller, J. E. Westcott, X. Sheng, and N. F. Krebs. 2010. Zinc bioavailability and homeostasis. *The American Journal of Clinical Nutrition* 91 (5):1478S–83S. doi: 10.3945/ajcn.2010.28674I.

Hambidge, K. M., N. F. Krebs, J. L. Westcott, L. Sian, L. V. Miller, K. L. Peterson, and V. Raboy. 2005. Absorption of calcium from Tortilla meals prepared from low-phytate maize. *The American Journal of Clinical Nutrition* 82 (1):84–7. doi: 10.1093/ajcn.82.1.84.

Hedrén, E., V. Diaz, and U. Svanberg. 2002. Estimation of carotenoid accessibility from carrots determined by an in vitro digestion method. *European Journal of Clinical Nutrition* 56 (5):425–30. doi: 10.1038/sj.ejcn.1601329.

Hermans, W. J. H., C. J. Fuchs, F. K. Hendriks, L. H. P. Houben, J. M. Senden, L. B. Verdijk, and L. J. C. van Loon. 2022. Cheese ingestion increases muscle protein synthesis rates both at rest and during recovery from exercise in healthy, young males: A randomized parallel-group trial. *The Journal of Nutrition* 152 (4):1022–30. doi: 10.1093/jn/nxac007.

Herreman, L., P. Nommensen, B. Pennings, and M. C. Laus. 2020. Comprehensive overview of the quality of plant- and animal-sources proteins based on the digestible indispensable amino acid score. *Food Science & Nutrition* 8 (10):5379–91. doi: 10.1002/fsn3.1809.

Hess, J. M., M. E. Comeau, S. Casperson, J. L. Slavin, G. H. Johnson, M. Messina, S. Raatz, A. J. Scheett, A. Bodensteiner, and D. G. Palmer. 2023. Dietary Guidelines Meet NOVA: Developing a menu for a healthy dietary pattern using ultra-processed foods. *The Journal of Nutrition* 153 (8):2472–81. doi: 10.1016/j.tjnut.2023.06.028.

Hjerpsted, J., E. Leedo, and T. Tholstrup. 2011. Cheese intake in large amounts lowers LDL-cholesterol concentrations compared with butter intake of equal fat content. *The American Journal of Clinical Nutrition* 94 (6):1479–84. doi: 10.3945/ajcn.111.022426.

Hulett, N. A., R. L. Scalzo, and R. E. B. Reusch. 2022. Glucose uptake by skeletal muscle within the contexts of type 2 diabetes and exercise: An integrated approach. *Nutrients* 14 (3):647. doi: 10.3390/nu14030647.

Hunter, G. R., H. Singh, S. J. Carter, D. R. Bryan, and G. Fisher. 2019. Sarcopenia and its implications for metabolic health. *Journal of Obesity* 2019:8031705–10. doi: 10.1155/2019/8031705.

Institute of Medicine [IOM]. 2001. *Dietary reference intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium and Zinc*. Washington, DC: National Academy Press.

Jenkins, D. J. A., and W. C. Willet. 2024. Perspective on the health value of carbohydrate-rich foods: Glycemic index and load; fiber and whole grains. *The American Journal of Clinical Nutrition* 120 (3):468–70. doi: 10.1016/j.ajcnut.2024.07.004.

Jenkins, D. J., M. J. Thorne, T. M. Wolever, A. L. Jenkins, A. V. Rao, and L. U. Thompson. 1987. The effect of starch-protein interaction in wheat on the glycemic response and rate of in vitro digestion. *The American Journal of Clinical Nutrition* 45 (5):946–51. doi: 10.1093/ajcn/45.5.946.

Karković Marković, A., J. Torić, M. Barbarić, and C. Jakobušić Brala. 2019. Hydroxytyrosol, tyrosol and derivatives and their potential effects on human health. *Molecules (Basel, Switzerland)* 24 (10):2001. doi: 10.3390/molecules24102001.

Katz, K. A., M. H. Mahlberg, P. J. Honig, and A. C. Yan. 2005. Rice nightmare: Kwashiorkor in 2 Philadelphia-area infants fed rice dream beverage. *Journal of the American Academy of Dermatology* 52 (5 Suppl 1):S69–S72. doi: 10.1016/j.jaad.2004.07.056.

Kerstetter, J. E., K. O. O'Brien, D. M. Caseria, D. E. Wall, and K. L. Insogna. 2005. The impact of dietary protein on calcium absorption and kinetic measures of bone turnover in women. *The Journal of Clinical Endocrinology and Metabolism* 90 (1):26–31. doi: 10.1210/jc.2004-0179.

Kim, J. E., M. G. Ferruzzi, and W. W. Campbell. 2016. Egg consumption increased vitamin E absorption from co-consumed raw mixed vegetables in healthy young men. *The Journal of Nutrition* 146 (11):2199–205. doi: 10.3945/jn.116.236307.

Kim, J. E., S. L. Gordon, M. G. Ferruzzi, and W. W. Campbell. 2015. Effects of egg consumption on carotenoid absorption from co-consumed, raw vegetables. *The American Journal of Clinical Nutrition* 102 (1):75–83. doi: 10.3945/ajcn.115.111062.

Lacroix, M., C. Bon, C. Bos, J. Léonil, R. Benamouzig, C. Luengo, J. Fauquant, D. Tomé, and C. Gaudichon. 2008. Ultra high temperature treatment, but not pasteurization, affects the postprandial kinetics of milk proteins in humans. *The Journal of Nutrition* 138 (12):2342–7. doi: 10.3945/jn.108.096990.

Lamothe, S., M.-M. Corbeil, S. L. Turgeon, and M. Britten. 2012. Influence of cheese matrix on lipid digestion in a simulated gastro-intestinal environment. *Food & Function* 3 (7):724–31. doi: 10.1039/c2fo10256k.

Lamothe, S., N. Rémillard, J. Tremblay, and M. Britten. 2017. Influence of dairy matrices on nutrient release in a simulated gastrointestinal environment. *Food Research International (Ottawa, ON)* 92:138–46. doi: 10.1016/j.foodres.2016.12.026.

Le Louer, B., J. Lemale, K. Garcette, C. Orzechowski, A. Chalvon, J.-P. Girardet, and P. Tounian. 2014. Severe nutritional deficiencies in young infants with inappropriate plant milk consumption. *Archives de Pediatrie: Organe Officiel de la Societe Francaise de Pediatrie* 21 (5):483–8. doi: 10.1016/j.arcped.2014.02.027.

Loewen, A., B. Chan, and E. C. Y. Li-Chan. 2018. Optimization of vitamins A and D3 loading on stability of vitamin D3 during storage. *Food Chemistry* 240:472–81. doi: 10.1016/j.foodchem.2017.07.126.

Lorenz, K., and B. D'Appolonia. 1980. Cereal sprouts: Composition, nutritive value, food applications. *Critical Reviews in Food Science and Nutrition* 13 (4):353–85. doi: 10.1080/10408398009527295.

Lorenzen, J. K., and A. Astrup. 2011. Dairy calcium intake modifies responsiveness of fat metabolism and blood lipids to a high-fat diet. *The British Journal of Nutrition* 105 (12):1823–31. doi: 10.1017/S0007114510005581.

Malapert, A., V. Tomao, M. Margier, M. Nowicki, B. Gleize, O. Dangles, and E. Reboul. 2018. β-Cyclodextrin does not alter the bioaccessibility and the uptake by caco-2 cells of olive by-product phenolic compounds. *Nutrients* 10 (11):1653. doi: 10.3390/nu10111653.

Melse-Boonstra, A. 2020. Bioavailability of micronutrients from nutrient-dense whole foods: Zooming in on dairy, vegetables, and fruits. *Frontiers in Nutrition* 7:101. doi: 10.3389/fnut.2020.00101.

Miller, L. V., N. F. Krebs, and K. M. Hambidge. 2007. A mathematical model of zinc absorption in humans as a function of dietary zinc and phytate. *The Journal of Nutrition* 137 (1):135–41. doi: 10.1093/jn/137.1.135.

Mogire, R. M., J. M. Muriuki, A. Morovat, A. J. Mentzer, E. L. Webb, W. Kimita, F. M. Ndungu, A. W. Macharia, C. L. Cutland, S. B. Sirima, et al. 2022. Vitamin D deficiency and its association with iron deficiency in African children. *Nutrients* 14 (7):1372. doi: 10.3390/nu14071372.

Monteiro, C. A., G. Cannon, J. C. Moubarac, R. B. Lev, M. L. C. Louzada, and P. C. Jaime. 2018. The UN Decade of Nutrition, the NOVA food classification and the trouble with ultra-processing. *Public Health Nutrition* 21 (1):5–17. doi: 10.1017/S1368980017000234.

Moore, S. S., A. Costa, M. Pozza, C. M. Weaver, and M. De Marchi. 2024. Nutritional scores of milk and plant-based alternatives and their difference in contribution to human nutrition. *LWT* 191:115688. doi: 10.1016/j.lwt.2023.115688.

Mozaffarian, D. 2016. Dietary and policy priorities for cardiovascular disease, diabetes, and obesity: A comprehensive review. *Circulation* 133 (2):187–225. doi: 10.1161/CIRCULATIONAHA.115.018585.

Mulet-Cabero, A.-I., M. Torres-Gonzalez, J. Geurts, A. Rosales, B. Farhang, C. Marmonier, E. K. Ulleberg, E. Hocking, I. Neiderer, I. Gandolfi, et al. 2024. The dairy matrix: Its Importance, definition, and current application in the context of nutrition and health. *Nutrients* 16 (17):2908. doi: 10.3390/nu16172908.

Muleya, M., E. F. Bailey, and E. H. Bailey. 2024. A comparison of bioaccessible calcium supplies of various plant-based products relative to bovine milk. *Food Research International (Ottawa, ON)* 175:113795. doi: 10.1016/j.foodres.2023.113795.

Nickel, K. P., B. R. Martin, D. L. Smith, J. B. Smith, G. D. Miller, and C. M. Weaver. 1996. Calcium bioavailability from bovine milk and dairy products in premenopausal women using intrinsic and extrinsic labeling techniques. *The Journal of Nutrition* 126 (5):1406–11. doi: 10.1093/jn/126.5.1406.

Nishimura, T. 2010. The role of intramuscular connective tissue in meat texture. *Animal Science Journal = Nihon Chikusan Gakkaiho* 81 (1):21–7. doi: 10.1111/j.1740-0929.2009.00696.x.

O'Connor, A., M. Rooney, S. Dunne, N. Bhargava, C. Matthews, S. Yang, S. Zhou, A. Cogan, J. J. Sheehan, A. Brodkorb, et al. 2024. An examination of the impact of unmelted, melted, and deconstructed cheese on lipid metabolism: A 6-week randomised trial. *Food & Function* 15 (16):8345–55. doi: 10.1039/D4FO02708F.

Ojo, O., O. O. Ojo, F. Adebowale, and X. H. Wang. 2018. The effect of dietary glycaemic index on glycaemia in patients with type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. *Nutrients* 10 (3):373. doi: 10.3390/nu10030373.

Phillips, S. M. 2017. Current concepts and unresolved questions in dietary protein requirements and supplements in adults. *Frontiers in Nutrition* 4:13. Erratum in: Front Nutr. 2023 Apr 12;9:1078528. doi: 10.3389/fnut.2022.1078528. PMID: 28534027; PMCID: PMC5420553. doi: 10.3389/fnut.2017.00013.

Romulo, A. 2022. Nutritional contents and processing of plant-based milk: A review. *IOP Conference Series: Earth and Environmental Science* 998 (1):012054. doi: 10.1088/1755-1315/998/1/012054.

Rutherfurd, S. M., N. M. Torbatinejad, and P. J. Mough. 2006. Available (Ileal digestible reactive) lysine in selected cereal-based food products. *Journal of Agricultural and Food Chemistry* 54 (25):9453–7. doi: 10.1021/jf061230l.

Scientific Advisory Committee on Nutrition. 2023. SACN Statement on processed foods and health. Available at: https://www.gov.uk/government/publications/sacn-statement-on-processed-foods-and-health

Serafini, M., M. R. Testa, D. Villaño, M. Pecorari, K. Van Wieren, E. Azzini, A. Brambilla, and G. Maian. 2009. Antioxidant activity of blueberry fruit is impaired by association with milk. *Free Radical Biology & Medicine* 46 (6):769–74. doi: 10.1016/j.freeradbiomed.2008.11.023.

Servili, M., B. Sordini, S. Esposto, S. Urbani, G. Veneziani, I. Di Maio, R. Selvaggini, and A. Taticchi. 2013. Biological activities of phenolic compounds of extra-virgin olive oil. *Antioxidants (Basel, Switzerland)* 3 (1):1–23. doi: 10.3390/antiox3010001.

Smith, N. W., A. J. Fletcher, J. P. Hill, and W. C. McNabb. 2021. Modeling the contribution of milk to global nutrition. *Frontiers in Nutrition* 8:716100. doi: 10.3389/fnut.2021.716100.

Taylor, J. R. N., M. Naushad Emmambux, and J. Kruger. 2015. Developments in modulating glycaemic response in starchy cereal foods. *Starch - Stärke* 67 (1–2):79–89. doi: 10.1002/star.201400192.

Teicholz, N. 2023. A short history of saturated fat: The making and unmaking of a scientific consensus. *Current Opinion in Endocrinology, Diabetes, and Obesity* 30 (1):65–71. doi: 10.1097/MED.0000000000000791.

Thorning, T. K., H. C. Bertram, J. P. Bonjour, L. de Groot, D. Dupont, E. Feeney, R. Ipsen, J. M. Lecerf, A. Mackie, M. C. McKinley, et al. 2017. Whole dairy matrix or single nutrients in assessment of health effects: Current evidence and knowledge gaps. *The American Journal of Clinical Nutrition* 105 (5):1033–45. doi: 10.3945/ajcn.116.151548.

Thorning, T. K., N. T. Bendsen, S. K. Jensen, Y. Ardö, T. Tholstrup, A. Astrup, and A. Raben. 2015. Cheddar cheese ripening affects plasma nonesterified fatty acids and serum insulin concentrations in growing pigs. *The Journal of Nutrition* 145 (7):1453–8. doi: 10.3945/jn.115.210716.

Toba, Y., K. Kato, Y. Takada, M. Tanaka, T. Nakano, T. Aoki, and S. Aoe. 1999. Bioavailability of milk micellar calcium phosphate-phosphopeptide complex in rats. *Journal of Nutritional Science and Vitaminology* 45 (3):311–23. doi: 10.3177/jnsv.45.311.

Trumbo, P. R., R. Bleiweiss-Sande, J. K. Campbell, E. Decker, A. Drewnowski, J. W. Erdman, M. G. Ferruzzi, C. G. Forde, M. J. Gibney, J. M. Hess, et al. 2024. Toward a science-based classification of processed foods to support meaningful research and effective health policies. *Frontiers in Nutrition* 11:1389601. doi: 10.3389/fnut.2024.1389601.

Tuck, K. L., M. P. Freeman, P. J. Hayball, G. L. Stretch, and L. Stupans. 2001. The in vivo fate of hydroxytyrosol and tyrosol, antioxidant phenolic constituents of olive oil, after intravenous and oral dosing of labelled compounds to rats. *The Journal of Nutrition* 131 (7):1993–6. doi: 10.1093/jn/131.7.1993.

U.S. Department of Agriculture (USDA). 2023. FoodData Central: USDA global branded food products database. Agricultural Research Service. fdc.nal.usda.gov.

Uwaezuoke, S. N. 2017. Vitamin D deficiency and anemia risk in children: A review of emerging evidence. *Pediatric Health, Medicine and Therapeutics* 8:47–55. doi: 10.2147/PHMT.S129362.

Uwitonze, A. M., and M. S. Razzaque. 2018. Role of magnesium in vitamin D activation and function. *Journal of the American Osteopathic Association* 118:81–189.

Vega-López, S., B. J. Venn, and J. L. Slavin. 2018. Relevance of the glycemic index and glycemic load for body weight, diabetes, and cardiovascular disease. *Nutrients* 10 (10):1361. doi: 10.3390/nu10101361.

Vissers, L. E. T., J. Rijksen, J. M. A. Boer, W. M. M. Verschuren, Y. T. van der Schouw, and I. Sluijs. 2019. Fatty acids from dairy and meat and their association with risk of coronary heart disease. *European Journal of Nutrition* 58 (7):2639–47. doi: 10.1007/s00394-018-1811-1.

Vogtschmidt, Y. D., S. S. Soedamah-Muthu, F. Imamura, D. I. Givens, and J. A. Lovegrove. 2024. Replacement of saturated fatty acids from meat by dairy sources in relation to incident cardiovascular disease: The European Prospective Investigation into Cancer and Nutrition (EPIC)-Norfolk Study. *The American Journal of Clinical Nutrition* 119 (6):1495–503. doi: 10.1016/j.ajcnut.2024.04.007.

Wall, B. T., N. M. Cermak, and L. J. C. Van Loon. 2014. Dietary protein considerations to support active aging. *Sports Medicine (Auckland, NZ)* 44 Suppl 2 (Suppl 2):S185–S194. doi: 10.1007/s40279-014-0258-7.

Weaver, C. M. 2021. Dairy matrix: Is the whole greater than the sum of the parts? *Nutrition Reviews* 79 (Suppl 2):4–15. doi: 10.1093/nutrit/nuab081.

Weaver, C. M., J. Dwyer, V. L. Fulgoni, 3rd, J. C. King, G. A. Leveille, R. S. MacDonald, J. Ordovas, and D. Schnakenberg. 2014. Processed foods: Contributions to nutrition. *The American Journal of Clinical Nutrition* 99 (6):1525–42. doi: 10.3945/ajcn.114.089284.

Weaver, C. M., M. Wastney, A. Fletcher, and K. Lividini. 2024. An algorithm to assess calcium bioavailability from foods. *The Journal of Nutrition* 154 (3):921–7. doi: 10.1016/j.tjnut.2023.12.005.

Wolfe, R. R., S. M. Rutherfurd, I. Y. Kim, and P. J. Moughan. 2016. Protein quality as determined by a digestible indispensable amino acid score: Evaluation of factors underlying the calculation. *Nutrition Reviews* 74 (9):584–99. doi: 10.1093/nutrit/nuw022.

Ye, A., J. Cui, D. Dalgleish, and H. Singh. 2017. Effect of homogenization and heat treatment on the behavior of protein and fat globules during gastric digestion of milk. *Journal of Dairy Science* 100 (1):36–47. doi: 10.3168/jds.2016-11764. 27837978.

Zaromskyte, G., K. Prokopidis, T. Ioannidis, K. D. Tipton, and O. C. Witard. 2021. Evaluating the leucine trigger hypothesis to explain the post-prandial regulation of muscle protein synthesis in young and older adults: A systematic review. *Frontiers in Nutrition* 8:685165. doi: 10.3389/fnut.2021.685165.

Zhao, Y., B. R. Martin, and C. M. Weaver. 2005. Calcium bioavailability of calcium carbonate fortified soymilk is equivalent to cow's milk in young women. *The Journal of Nutrition* 135 (10):2379–82. doi: 10.1093/jn/135.10.2379.

Zielbauer, B. I., J. Franz, B. Viezens, and T. A. Vilgis. 2016. Physical aspects of meat cooking: Time dependent thermal protein denaturation and water loss. *Food Biophysics* 11 (1):34–42. doi: 10.1007/s11483-015-9410-7.

Zrelli, H., M. Matsuoka, S. Kitazaki, M. Zarrouk, and H. Miyazaki. 2011. Hydroxytyrosol reduces intracellular reactive oxygen species levels in vascular endothelial cells by upregulating catalase expression through the AMPK-FOXO3a pathway. *European Journal of Pharmacology* 660 (2–3):275–82. doi: 10.1016/j.ejphar.2011.03.045.