Nutrition 30 (2014) 619–627

Contents lists available at ScienceDirect

Nutrition

journal homepage: www.nutritionjrnl.com

Review

# Milk nutritional composition and its role in human health

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ARTICLE INFO

*Article history:*
Received 16 August 2013
Accepted 21 October 2013

*Keywords:*
Dairy
Protein
Calcium
Bone mass
Lactose intolerance
Healthy diet

ABSTRACT

Dairy and milk consumption are frequently included as important elements in a healthy and balanced diet. It is the first food for mammals and provides all the necessary energy and nutrients to ensure proper growth and development, being crucial in respect to bone mass formation. However, several controversies arise from consumption of dairy and milk products during adulthood, especially because it refers to milk from other species. Despite these controversies, epidemiologic studies confirm the nutritional importance of milk in the human diet and reinforce the possible role of its consumption in preventing several chronic conditions like cardiovascular diseases (CVDs), some forms of cancer, obesity, and diabetes. Lactose malabsorption symptoms and cow milk protein allergy are generally considered to be the adverse reactions to milk consumption. The present article reviews the main aspects of milk nutritional composition and establishes several associations between its nutritious role, health promotion, and disease prevention.



Mammalian milk is the first food for mammals and as such supplies all the energy and nutrients needed to ensure proper growth and development in the postnatal period. Milk consumption generally stops after the end of the weaning period, except in humans, as it is ingested even during adulthood.

Dairy foods in general are commonly considered balanced and nutritive foods, being frequently included as important components of a healthy diet. The present review will address the chemical composition of milk and the functional properties of its components, as well as the effect of milk consumption on human health.

## Milk composition

To our knowledge, although there are several milk products, the general term *milk* should only refer to cow's milk, produced by healthy animals and excluding the lactic secretion between 15 d before and 5 d after labor, or until it is almost completely free of colostrum [1]. This definition should exclude completely the so-called milk products of vegetable origin like "soy milk," "almond milk," etc. These should be called "beverages" according to their origin, such as "soy beverage," as previewed in the European Union legislation [2].

The chemical composition of milk can be influenced by several factors such as animal species and genetics, environmental conditions, lactation stage, and animal nutritional status [3,4]. Although cow milk is probably the most frequently consumed, sheep and goat milk also can be found. When comparing cow milk with those, as well as with human milk, which had been considered the perfect food for infants [5], some differences can be pointed out. In comparative reviews, Park [6], Jandal [7] and Raynal et al. [8] had reported that sheep milk can be distinguished by its higher protein and fat content while goat milk had presented higher amount of A, B1 and B12 vitamins as well as calcium and phosphorus content when compared to cow and sheep milk. These data are presented in Table 1.

### *Chemical composition*

On average, bovine milk is composed of 87% water, 4% to 5% lactose, 3% protein, 3% to 4% fat, 0.8% minerals, and 0.1% vitamins [9,10].

### *Milk proteins*

Milk is generally considered an important protein source in the human diet, supplying approximately 32 g protein/L. Its protein fraction can be divided into soluble and insoluble proteins. Soluble proteins, named whey proteins, represent 20% of milk protein fraction, whereas the insoluble, namely caseins, represent 80% [9,11]. Both are classified as high-quality proteins considering human amino acid requirements, digestibility, and bioavailability. In fact, milk proteins are frequently considered the best protein source taking in to account the essential amino

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0899-9007/$ - see front matter 
http://dx.doi.org/10.1016/j.nut.2013.10.011

**Table 1**
Average composition of goat, sheep, cow, and human milk

| | Goat | Sheep | Cow | Human |
|---|---|---|---|---|
| Fat (%) | 3.8 | 7.9 | 3.6 | 4.0 |
| Lactose (%) | 4.1 | 4.9 | 4.7 | 6.9 |
| Protein (%) | 3.4 | 6.2 | 3.2 | 1.2 |
| Energy (kcal/100 mL) | 70 | 105 | 69 | 68 |
| Calcium (mg/100 g) | 134 | 193 | 122 | 33 |
| Phosphorus (mg/100 g) | 121 | 158 | 119 | 43 |
| Vitamin A (IU) | 185 | 146 | 126 | 190 |
| Vitamin D (IU) | 2.3 | 0.18 (μg) | 2.0 | 1.4 |

Adapted from [6,7]

acid score and protein-digestibility corrected amino acid score [12,13]. The amino acid profile is quite different between the two fractions: Whey is especially rich in branched chain amino acids, i.e., leucine, isoleucine, and valine as well as lysine, whereas casein has a higher proportion of histidine, methionine, and phenylalanine [14].

Apart from the high-quality and biological value, milk proteins and several bioactive peptides resulting from their enzymatic hydrolysis have shown multiple biological roles that could exert a protective action in human health. These main biological actions include antibacterial, antiviral, antifungal, antioxidant, antihypertensive, antimicrobial, antithrombotic, opioid, and immunomodulatory roles, in addition to improving absorption of other nutrients [15], and are briefly summarized in Table 2.

*Functional role of whey proteins.* The soluble protein fraction includes the following proteins: β-lactoglobulin, α-lactoalbumin, immunoglobulins (Ig) serum albumin, lactoferrin, lactoperoxidase, lysozyme, proteose-peptone, and transferrin [11]. Lactoferrin, lactoperoxidase, and lysozyme are important antimicrobial agents [16–18], whereas lactoferrin together with β-lactoglobulin and α-lactoalbumin has shown suppressing action in tumor development [19].

β-lactoglobulin is an important retinol carrier, and has shown fatty acid-binding action and antioxidant capacities, whereas lactoferrin is a crucial element in iron absorption and in exerting antioxidant and anticarcinogenic effects [15,20].

It is important to note that Igs are transferred from placenta to the fetus, which justifies the low concentrations after birth. Their most important source is colostrum, from which they are absorbed by infants to guarantee immunity defenses after birth. Human milk mainly contains IgA, colostrums have 100 times more Igs than milk [1,21].

*Functional role of caseins.* The main role attributed to caseins is mineral binding and their capacity as carriers, mainly for calcium and phosphorus. Total caseins can be divided in α-, β-, and κ-caseins. They transport calcium and phosphorus, forming a coagulum and improving their digestibility in the stomach [22].

Additionally, caseins give origin to several bioactive peptides that have shown benefits in human health. These include antioxidant [23,24], cytomodulatory, immunomodulatory [21], antihypertensive [25], and antithrombotic actions [26] in the cardiovascular, nervous, immune, and digestive systems. Some peptides like β-casomorphines have opioid-like actions, working similar to an analgesic and tranquilizer that affects the central nervous system [27]. Experimental studies also have shown that some peptides interfere in the gastrointestinal (GI) tract by promoting mucin production, thus preventing pathogen adherence to the intestinal surface, causing effects in intestinal motility that can justify a possible role in weight control through regulating food intake [28,29].

*Fatty acid composition*

Fat fraction in milk is mainly present in globules that are resistant to pancreatic lipolysis unless they are first submitted to gastric digestion [30]. Triacylglycerol (TAG) forms 98% of milk fat fraction, whereas other lipids like diacylglycerol (2%), cholesterol (< 0.5%), phospholipids (∼1%), and free fatty acids (0.1%) also can be found. Additionally, there are trace amounts of hydrocarbons, fat-soluble vitamins, flavor compounds, and other ingredients introduced through the animal feed. Milk fat is the most complex of all natural fats considering that more than 400 different fatty acids form its TAGs [31].

Amount and composition of milk fatty acid depend on animal origin, stage of lactation, mastitis, ruminal fermentation, or feed-related factors. In fact, milk fatty acids are derived either from feed or from the microbial activity in the rumen. On average, 70% of fat fraction is composed by saturated fatty acids (SFAs) and 30% unsaturated fatty acids. Within SFAs, the most important from a quantitative viewpoint are palmitic (30%), myristic (11%), and stearic (12%). Short-chain fatty acids also can be found and make up 11% of SFAs, mainly butyric (4.4%) and caproic (2.4%) [10,31].

In the unsaturated fatty acid fraction, oleic acid is present in concentrations within 24% to 35%, whereas polyunsaturated fatty acids constitute around 2.3% of total fatty acids, with linoleic and α-linolenic accounting for 1.6% and 0.7%, respectively. Milk also includes trans-fatty acids like vaccenic acid (2.7%) and conjugated linoleic acid (0.34%–1.37%) [10,31].

**Table 2**
Biological functions and concentrations of the main milk proteins

| Protein | Concentration (g/L) | | Function |
|---|---|---|---|
| | Cow | Human | |
| Total caseins | 26.0 | 2.7 | Mineral transport (Ca, PO4, Fe, Zn, Cu) |
| α-Casein | 13.0 | | |
| β-Casein | 9.3 | | |
| κ-Casein | 3.3 | | |
| Total whey proteins | 6.3 | 67.3 | |
| β-Lactoglobulin | 3.2 | | Retinol and fatty acid binding; possible antioxidant |
| α-Lactoalbumin | 1.2 | 1.9 | Lactose production, calcium transport, immunomodulator; anticarcinogen |
| Immunoglobulin (IgA, IgM, IgE, IgG) | 0.7 | 1.3 | Immune protection |
| Serum albumin | 0.4 | 0.4 | |
| Lactoferrin | 0.1 | 1.5 | Antimicrobian, antioxidant, immunomodulator, iron absorption, anticarcinogen |
| Lactoperoxidase | 0.03 | | Antimicrobian |
| Lysozyme | 0.0004 | 0.1 | Antimicrobian, synergy actions with immunoglobulins and lactoferrin |
| Others | 0.8 | 1.1 | |
| Proteose-peptone | 1.2 | | |
| Glycomacropeptides | 1.2 | | Antiviral, bifidogen |

Adapted from [13,103]

**Table 3**
Average nutritional composition of whole, low-fat, and skim milk (UHT)

| Composition (100 g) | Whole | Low-fat | Skim |
|---|---|---|---|
| Energy (kcal) | 62 | 47 | 34 |
| Water (g) | 88.1 | 89.1 | 90.5 |
| Protein (g) | 3 | 3.4 | 3.3 |
| Fat (g) | 3.5 | 1.6 | 0.2 |
| Carbohydrates (g) | 4.7 | 4.9 | 4.9 |
| Cholesterol (mg) | 13 | 8 | 1 |
| Vitamin A (mg) | 59 | 22 | 0 |
| Vitamin D (mg) | 0.05 | 0.05 | 0 |
| Vitamin $B_1$ (mg) | 0.04 | 0.04 | 0.05 |
| Vitamin $B_2$ (mg) | 0.14 | 0.11 | 0.05 |
| Na (mg) | 43 | 41 | 41 |
| Ca (mg) | 109 | 112 | 114 |
| Mg (mg) | 9 | 9 | 10 |

Ca, calcium; Mg, magnesium; Na, sodium; UHT, ultra-high temperature
Adapted from [104]

The term, *conjugated linoleic acid* (CLA), commonly refers to a group of octadecadienoic isomers derived from linoleic acid, which result from biohydrogenation reactions performed by ruminant animal's GI microbes. This group of fatty acids has deserved additional attention due to its health benefits in the cardiovascular system and immune function, as well as in its anticancer properties and hypolipidemic effects [32,33]. Within the several compounds included, the *cis*-9, *trans*-11, and the *trans*-10, *cis*-12 isomers are considered the most active [15,33]. The CLA amount in milk can be quite variable mainly due to season and as a consequence of animal nutrition [34]. Nevertheless, dairy products account for 70% of the CLA ingested daily [35].

In regard to milk classification according to fat content, since 1980 the dairy industry had been adapting milk to consumer need and interest. The search for less-caloric products has forced the creation of new strategies to ensure nutritional richness, proper flavor, texture, and odor with lower fat and thus lower energy content. Table 3 presents the average nutritional composition comparing whole, low-fat, and skim milk.

*Vitamins and minerals*

Dairy products in general and especially milk, as their raw material, have a particular micronutrient composition. Milk has been naturally recognized as a privileged calcium source but in its mineral fraction, several other elements can be distinguished such as phosphorus, magnesium, zinc, and selenium [36]. The vitamin fraction is composed by liposoluble vitamins A, D, and E and also by water-soluble B complex vitamins such as thiamine and riboflavin.

*Mineral fraction.* Calcium is naturally the macroelement present in higher amounts in milk. The average concentration of calcium is 1200 mg/L of milk which is distributed between the micellar and aqueous phases. In the micellar phase, it is associated with the phosphoseryl residues of caseins, whereas in the aqueous phase, calcium can bind to whey proteins or inorganic forms of phosphate-forming salts [37,38].

These phases are in thermodynamic equilibrium but if changes occur in the physicochemical milk conditions, such as pH and temperature, this could lead to the passage of calcium molecules from one phase to another.

In addition to calcium, milk is also recognized as a good source of phosphorus, which is present in organic and inorganic forms. Organic phosphate is bound to organic molecules like proteins, phospholipids, organic acids, and nucleotides, which are present mainly in the micellar phase; whereas the inorganic form corresponds to the ionized phosphate, which depends on the pH value and is located in the aqueous phase. Similar to calcium, both forms are in equilibrium and their distribution may depend on conditions like pH. The average concentration of phosphorus in milk is about 950 mg/L [36].

**Table 4**
Average mineral content in milk compared with dietary reference intakes

| Mineral | mg/100 g | Amount in 1 cup (244 g) and % DRI | |
|---|---|---|---|
| Calcium | 119–124 | 297.50–310 | 37–40 |
| Phosphorus | 93–101 | 232.50–252.5 | 16–32 |
| Magnesium | 11–14 | 27.5–35 | 8–10 |
| Potassium | 151–166 | 377.5–415 | 8–9 |
| Zinc | 0.4–0.6 | 1–1.5 | 9–14 |

DRI, dietary recommended intake
Adapted from [10,36,41]

Although not so abundant, magnesium also can be found in milk as well as in other dairy products. As happens to calcium and phosphorus, the dynamic equilibrium between the micellar and aqueous phases is sensitive to conditions like pH [36]. One L of milk supplies 120 mg of magnesium, which corresponds to 29% of the dietary reference intake for this mineral [39].

Milk is also a good source of microelements like zinc and selenium. One L of milk supplies 3 to 4 mg of zinc, which is mostly present in the micellar phase associated with casein [40]. Selenium is present in an average concentration of 30 μg/L, which represents around 67% of the dietary reference intake for this oligoelement [41]. The average milk mineral composition is presented in Table 4.

## Vitamin content in milk

The milk vitamin profile includes liposoluble (A, D, E) and hydrosoluble vitamins (B complex and vitamin C) [9,36].

The concentrations of fat-soluble vitamins in milk depend on milk fat content, thus low-fat and skim milk varieties have lower amounts of A, D, and E vitamins. In some countries, skim milk is fortified with A and D vitamins to improve its nutritional richness.

Vitamin A is especially important in growth, development, immunity, and eye health. Its content in milk depends mainly on fat amount, but also on factors like animal feed and season [36]. Whole milk is generally considered a good vitamin A source, supplying around 172 μg/100 g; however, vitamin A content in skim or fat-free milk can be as low as 102 μg/100 g and 5 μg/100 g, respectively [10,42]. Thus, several countries have chosen to fortify fat-reduced milk products to improve nutritional status and reduced vitamin A deficiency, especially in children [43].

Despite being globally considered a good source, milk itself does not present considerable amounts of vitamin D except when fortified. Previous studies have reported values within 5 and 35 IU/L [44], which is in accordance with reference nutritional tables. Commercially available whole milk, to which vitamin D is added, presents within 40 to 51 IU/100 g [10,42]. Recently, vitamin D started to deserve more attention as a polyvalent micronutrient considering some attributed protective actions. Studies have suggested vitamin D has anticarcinogenic [45,46], cardioprotective [47], and immunomodulatory [48] effects and nevertheless is crucial in calcium absorption, thus in bone mass formation, and can be determinant in the prevention of osteoporosis [49].

Milk can surely be distinguished by its richness in B complex vitamins, providing 10% to 15% of the daily recommended intake for most people (Table 5). These vitamins are important enzymatic cofactors and participate in several metabolic pathways

**Table 5**
Cow milk vitamin content and comparison with dietary recommended intakes

| Vitamin | /100 g | Amount in 1 cup (244 g) and % DRI | |
|---|---|---|---|
| $B_1$ (thiamin) | 0.04–0.05 mg | 0.091–0.1104 mg | 9.1–11 |
| $B_2$ (riboflavin) | 0.16–0.17 mg | 0.395–0.4514 mg | 35.9–0.41 |
| $B_3$ (niacin) | 0.08–0.09 mg | 0.204–0.229 mg | 1.7–1.9 |
| $B_6$ (piridoxin) | 0.04–0.04 mg | 0.089–0.105 mg | 8.0–9.5 |
| Folate | 5–5.2 µg | 12.2–12.688 µg | 3.8–4.0 |
| $B_{12}$ (cobalamin) | 0.357–0.500 µg | 0.871–1.22 µg | 36.3–61.0 |

DRI, dietary recommended intake
Adapted from [10,36,41]

like energy production from nutrients, neurotransmitter, and hormone synthesis [39].

## Organism adverse reactions to milk consumption

There are two main adverse reactions due to milk ingestion. On the one hand are lactose intolerance symptoms that can imply milk avoidance leading the individual to consume other dairy products with vestigial lactose content like yogurt and cheese. On the other hand, cow milk protein allergy implies a complete avoidance of cow milk products.

### *Lactose intolerance*

Lactose is the main carbohydrate present in milk. It is a disaccharide composed by glucose and galactose. It can be found in two isomeric forms, alfa (α) and beta (β) that in aqueous solution are in balance. It is hydrolyzed by a β-galactosidase known as lactase, which has a special preference for the β form [50]. This enzyme is connected to small intestine mucosa membrane and after lactose is hydrolyzed, the two monosaccharide glucose and galactose are absorbed and transported to the liver through the portal vein where galactose is converted to glucose [51]. In mammals, β-galactosidase activity decreases significantly after weaning; this apparently does not happen at the same grade in humans. Its activity remains even during adulthood and intolerance symptoms occur when, for some reason, there is an enzymatic deficiency.

The terminology used to define β-galactosidase deficiency and lactose intolerance has changed throughout time. In fact, several terms have been used to define different clinical symptoms [50].

Hippocrates (460–370 B.C.) first described lactose intolerance, but clinical symptoms were only recognized 50 y ago. Studies suggest that 70% of the world population have persistent β-galactosidase [52], but not all are lactose intolerance because several factors—nutritional and genetic—can influence its absorption [53,54].

Lactose intolerance itself causes several GI symptoms provoked by lactose and sugar fermentation in the colon. Abdominal cramps and bloating, flatulence, diarrhea, nausea, and vomiting are frequent adverse events. During fermentation several compounds are formed such as short-chain fatty acids, methane, and carbon dioxide, which also can affect intestinal motility causing constipation, increased bowel internal pressure, and increased bowel transit time [55].

The acidification of colonic content and increased osmotic pressure due to nonabsorbed lactose results in a great secretion of electrolytes and fluids in the colon, which accelerates intestinal transit and causes loose stools and diarrhea [56,57]. The amount of lactose that can cause these symptoms can vary within individuals, as well as with the consumption of other foods and the degree of β-galactosidase deficiency.

β-galactosidase deficiency is the natural cause of lactose intolerance and can be congenital if it is associated with minimal enzyme activity present since birth; a primary enzyme deficiency that can occur after weaning or can be acquired if it is due to enzyme activity loss like after a GI disease [58].

In addition to classic lactose intolerance symptoms, β-galactosidase deficiency can cause severe metabolic consequences. If a lactose-intolerant individual continues to ingest elevated doses of lactose, high levels of galactitol formed by reductase NADPH can cause blindness and be fatal because this conversion can occur in eye lenses or in neural tissue [50].

Some years ago, the only treatment possibility for lactose intolerance was avoidance of lactose products. However, some studies suggested that individuals with nonpersistent β-galactosidase can consume up to 11 g/d of lactose without adverse symptoms. It also has been shown that lactose digestion is improved by combination with other foods in small amounts and throughout the day [59]. Colon bacteria also can adapt their metabolic activity to improve lactose tolerance [56,57], such as through the consumption of lactic bacteria or specific probiotics [60].

### *Cow milk protein allergy*

Cow milk protein allergy is generally the first food allergy observed in children and its prevalence varies within 2% to 7.5% [61–63]. It can be characterized as an immunologic-mediated adverse reaction to cow milk protein and it can be developed in the neonatal period or during the first years of life. Normally, it tends to remit during childhood and is quite uncommon in adults [63].

Cow milk protein allergy can be associated to IgE reactions and the adverse consequences can be immediate (IgE-mediated) or delayed (non–IgE-mediated). The immediate reaction symptoms include anaphylaxis, cutaneous reactions with urticaria and edema, respiratory episodes, and GI distress including vomiting, diarrhea, and bloody stools [63,64]. Similarly, the late-onset phenomenon is also characterized by cutaneous, respiratory, and GI symptoms, including disorders like atopic dermatitis, milk-induced pulmonary disease, chronic diarrhea, and gastroesophageal reflux disease. These aftereffects can happen 1 h to several days after ingestion of cow milk. Most frequently, these allergies are due to whey proteins, mainly β-lactoglobulin, but also can be promoted by caseins [61–63].

Because they affect mainly children, including during the neonatal period, improper growth is a direct consequence and management guidelines are quite frequently addressed to ensure children adequately develop. In breast-fed infants, mothers are commonly advised to avoid all cow milk-derived products; whereas in formula-fed children, the alternative is to replace cow milk products for hydrolyzed or amino acid options. Some health professionals also recommend vegetable alternatives such as soy or rice formulas [65]. The option to use goat or sheep milk formulas can be ignored because of the similarity in protein structure, which can happen with other mammals; however, there is some evidence suggesting the possibility of using camel, swine, or equine milk [66].

Despite being rare, some cow milk allergy cases in adulthood can been found and clinical research has shown that symptoms are quite severe, even when compared with children, including respiratory and cardiovascular impairments, as well as some frequency of anaphylactic shock. Additionally, the necessary doses to provoke allergy aftereffects are lower. These have been mainly attributed to α-lactalbumin and β-lactoglobulin [67].

## Milk and health

Studies on milk consumption have shown a controversial and complex effect on human health. It is important to remember that humans are the only adult mammals who keep drinking milk after weaning, which raises some questions concerning the need of this habit. Some studies reinforce the role of dairy in general, milk included, as important macro and micronutrient sources, justifying its place in a healthy diet [68]; whereas others suggest a possible association of milk consumption with increased risk for several Western diseases such as CVD, diabetes, and cancer [69].

### *Milk consumption and cardiovascular disease*

Milk is a complex food, thus it is possible to find components that exert protective effects in cardiovascular health and others that can have a pejorative influence.

The main concern when referring to possible negative influence of milk consumption in heart disease has been related to its saturated fat content, which represents 70% of total milk fat as previously presented. An excessive consumption of saturated fat was previously associated with increased risk for CVD risk [70,71]. The most frequently proposed mechanism through which saturated fat influences risk for heart disease is by increasing blood lipids, especially total cholesterol (TC) and low-density lipoproteins (LDLs) [72].

However, the three main SFAs present in milk lipid fraction—palmitic, myristic and lauric—exert quite different metabolic effects in blood lipids, which can have complex effects in cardiovascular health. Palmitic acid has been shown to increase LDLs; myristic increases TC; and a high-density lipoprotein (HDL)-increasing effect had been attributed to lauric acid. Furthermore, stearic acid, which represents 12% of dairy fat decreases the TC to HDL, ratio which would have a protective action [73].

These would justify results obtained in several prospective cohort studies that included data regarding milk consumption previously to the 1980s, thus referring to whole milk as well as the conclusions presented in some recent meta-analyses and reviews where, to our knowledge, no convincing data was found suggesting a pejorative role of milk consumption in CVD risk regardless of fat content [74–78].

These results and conclusions are not free of controversy considering that in some studies differences were found within the relative risk from full-fat to low-fat milk versions concerning stroke [79] and brain hemorrhage [80], two very specific forms of CVD and brain vascular disease.

Reported specific metabolic differences within SFAs and the conclusions from the referred meta-analysis should not mean that whole milk consumption is free of risk and caution should be considered especially in high cardiovascular risk individuals and subgroups such as individuals with diabetes [81,82]. Nutritional guidelines and advisory boards have been recommending the option for reduced-fat milk versions.

Other milk components, such as minerals like calcium, magnesium, and potassium as previously described, also can influence cardiovascular health. These elements can exert a protective role in CVD due to their antihypertensive effect. The Rotterdam study found a 20% reduction in hypertension incidence associated with dairy consumption [83], and the combination of calcium, magnesium, and potassium has proven essential for blood pressure control [84]. This balance probably justifies why milk is superior in preventing hypertension when compared with mineral dietary supplements [85].

Nevertheless, dairy in general and especially milk also are recognized sources of bioactive peptides produced during casein digestion through the GI tract [86]. Several of these peptides directly inhibit the angiotensin-converting enzyme [87] from reducing the synthesis of the potent vasoconstrictor angiotensin II and the hydrolysis of bradykinin [88] with this, thus exerting a moderating role on blood pressure control.

Hypertension is a major risk factor for CVD [89] and dietary habits influence significantly its prevention and act as therapeutic coadjuvant. Several studies have reported a significant association between low-fat dairy consumption and risk for hypertension [83,90]. In fact, dairy products are frequently pointed out as important diet components in a considered healthy and cardioprotective food pattern broadly known and applied in hypertension treatment and prevention, the Dietary Approach to Stop Hypertension (DASH). DASH recommends a daily consumption of low-fat milk and other dairy products [91].

Considering all these factors, it is possible to suggest a potential protective influence of milk consumption in CVD. Despite the saturated fat content, to our knowledge there is no strong evidence demonstrating hazards from whole milk consumption due to specific and diverse metabolic effects of SFAs found in milk fat fraction. However, for caution, reduced-fat formulations should be considered especially in populations at higher risk for CVDs.

### *Milk consumption and cancer*

It is not completely clear if milk consumption increases or decreases the risk for cancer. Cancer has a complex and multifactorial etiology, thus there is no available evidence to prove the effect of a single food and/or nutrient on its origin and development. Moderate dairy product consumption has been recommended as a healthy food habit suggested as part of a protective dietary pattern involved in the prevention of several chronic diseases, including cancer [92].

Control and case–control studies have shown inverse associations or no effect of moderate milk consumption in colorectal [93,94], breast [95–97], prostate [98], and bladder [99] cancers.

However, this is not free from controversy. Some epidemiologic data [100] has shown an increased risk for cancer in higher quartiles of milk consumption.

Similar to what happens in CVD, some milk components can play a protective role in carcinogenesis, whereas others can promote this phenomenon and increase the risk for cancer.

The pejorative effect of milk consumption in risk for cancer has been most frequently attributed on the one hand to the presence of insulin-like growth factor (IGF)-1, and on the other hand to the fat content.

A systematic review [101] concluded that milk consumption is associated with increased values of IGF-1, based on several cross-sectional studies. IGF-1 has been associated with an increased risk for breast and prostate cancers [102,103].

The other milk component that is frequently identified as a carcinogenesis promoter is fat; this is mainly supported by experimental data [104]. Lipids are an important energy source and limiting their ingestion would potentially reduce energy resources that limit cancer cell proliferation [105]. However, this is a very simple mechanistic approach that cannot be fully applied considering whole milk has been associated with breast [106] and bladder cancers [107] but not with colorectal [108] and prostate [109] cancers.

Also, it is important to consider that excessive fat consumption may affect production of androgens and estrogens [110,111], which can be involved in prostate and breast carcinogenesis.

Somewhat apart from these explanations, a few studies addressed a possible pejorative role of lactose specifically in ovarian cancer [112,113] and calcium in prostate cancer [114,115].

Animal research has shown that galactose, resulting from lactose metabolism, can have a toxic effect on the ovaries and impair the normal gonadotropic secretion, which would be a promoter factor for carcinogenesis [116,117]. This may explain why other dairy products like yogurt and cheese have been associated with lower risk for ovarian cancer [118].

Concerning calcium, the suggested hypothesis is that excessive calcium intake impairs the synthesis of vitamin D and possibly promotes vitamin D receptor gene polymorphisms, which suppress its modulating role in prostate cell tumor growth and development [119–121].

Despite these data, the pejorative role of milk consumption is not observed in all cancer forms. Epidemiologic evidence has suggested that moderate milk consumption is associated with lower risk for colorectal cancer [94]. Calcium, folate, and vitamin D are the milk components most frequently discussed as being responsible for this protective effect, which may be due to the fact that these three micronutrients prosecute crucial actions in regulating cell proliferation affecting carcinogenesis process [122]. It is important to note folate's role in DNA methylation, which is the possible interplay between nutrient and cancer genetic etiology [123]. In fact, folate intake has been inversely associated with colorectal cancer in experimental and epidemiologic studies [124,125]. Calcium antiproliferative mechanisms may be explained through its role in secondary bile acids and ionized fatty acids that are proliferation promoters in colon epithelium [126,127].

Considering these data, it is possible to suggest that the complex etiology of cancer does not allow a clear and evident conclusion about a positive or negative role of milk consumption in risk for cancer; however, some assumptions can be made. Excessive milk consumption can increase prostate and ovarian cancers due to calcium and lactose intake, respectively. Whole-milk consumption also can increase risk for breast and prostate cancers due to the influence of fat in androgens and estrogens, as well as to the increased energy availability, which would facilitate carcinogenesis process. However, these associations are not common in all cancer forms; moderate milk consumption, regardless of fat content, has a protective effect in colorectal cancer.

### *Influence of milk consumption in weight gain, obesity, type 2 diabetes, and metabolic syndrome*

Few epidemiologic studies have addressed the possible effect of milk consumption in risk for type 2 diabetes. Results from the longest cohort study have shown that higher milk intake was associated with a reduced relative risk [74], which was confirmed by the most recent meta-analysis [74,128,129].

This protective effect may be due to milk's richness in calcium and magnesium, two minerals that have been found crucial in insulin sensitivity and glucose tolerance as reported in experimental and cohort studies, as well as in a recent meta-analysis [130–132].

In parallel, some hypothesis have suggested that milk whey proteins can exert interesting effects in glycemic control and insulin response, as well as in satiety, which would help decrease excessive food intake and thus prevent weight gain [133,134].

Additionally, milk proteins have proven helpful in satiety and appetite control mainly due to their effect in gut hormones like cholecystokinin and glucagon-like-peptide I [135,136], despite some controversial results reported previously [137]. Also, whey proteins have shown to decrease ghrelin [138,139].

A previous review [140] proposed a multifunctional effect for milk whey proteins in glucose tolerance and insulin sensitivity improvement, lower body weight and adiposity, better blood pressure control, and antioxidant and anti-inflammatory actions that would justify a protective role of these components in the prevention of metabolic syndrome (MetS), which also would contribute to lower risk for CVD.

The only negative factor in these findings is that most studies used whey protein powders and not milk. Because whey protein represents only 20% of milk protein fraction, its biological actions when consumed directly from milk can have a different effect on human health.

It has been suggested that whey proteins, calcium, and folate are the most important intervenient in preventing MetS due to their effects in appetite and satiety, glucose tolerance, insulin sensitivity, and blood pressure control [141]. Additionally, milk fatty acid profile and calcium content has proven quite favorable in lipid metabolism, with less small and dense LDL particles, lower plasma TAG and fasting insulin levels in addition to higher levels of HDL [142].

Another milk component that can prevent weight gain and adiposity is CLA. Experimental studies have shown significant effects of CLA intake in weight loss and whole-body composition [143–150]; however, human research has been inconclusive [151,152] despite some promising results effects [153]. It has been suggested that CLA reduces adiposity due to its effect on energy metabolism and on the adipogenesis itself, reducing inflammation, regulating lipid metabolism, and inducing apoptosis [154].

However, it should be noted that people who drink milk within the recommended amounts are more prone to maintain healthier food and lifestyle habits. This may be crucial to prevent weight gain and obesity, which are risk factors for CVD, diabetes, cancer, and MetS [155].

### *Milk consumption, calcium intake, and osteoporosis prevention*

The most frequent claim favorable to milk consumption has been its richness in calcium and this mineral's role in bone density [156]. Low bone mass is the main risk factor for osteoporosis and it is known that bone mass in later life is quite dependable from the peak bone mass achieved during growth [157,158].

Milk consumption has been previously associated with a higher bone density, which is protective [159]. This effect could be attributed only to calcium, but there is considerable debate concerning the effect of calcium supplementation by itself in bone mass [156].

In fact, one study [160] has suggested that milk supplies a varied array of minerals and other components like peptides and CLA, which could play a positive role in bone mass, lower prevalence of fractures, and osteoporosis prevention.

This can be supported by knowledge about nutrients that are thought to influence production and maintenance of bone matrix such as high biological value protein, vitamins C, D, and K, as well as minerals like copper, manganese, and zinc [78]. Nevertheless, calcium absorption can be influenced by some components and it is quite optimal in milk due to the presence of protein and lactose and the ratio of calcium and phosphorus [161–163].

For all these reasons milk intake is globally recommended as a promoter of good bone health [164].

## Concluding remarks

Milk is undoubtedly an omnipresent food in the human diet. It is the first food of mammals and the subject of several health claims. The constant association of milk consumption and a healthy diet has made milk a recommended food.

The nutritional richness of milk is unquestionable; it is a good source of high biological value proteins with polyvalent roles in immune function, as well as nutrient transport and absorption and important vitamins and essential minerals.

Despite some controversial recent hypotheses about the possible pejorative effects from milk consumption, adding up to lactose malabsorption and intolerance symptoms that would be natural in adulthood, no clear mechanisms and strong evidence have been found, leaving no clear argument to completely exclude a moderate consumption of milk.

Further studies should explore a clearer dose-response and the specific effects of milk fat in health and disease. Additionally, researchers seeking to determine the protective or harmful effects of milk in the diet should take into consideration the contributory role of food habits and lifestyle.

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