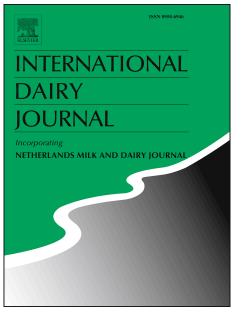

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Magnesium in milk

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ABSTRACT

This review draws attention to the significance of magnesium in milk, both the technical and human health aspects. Magnesium has been subject to less research than calcium in both aspects. Magnesium is present in cows' milk in ~10% of the concentration of calcium. About two-thirds of the magnesium is soluble, whereas about one third of calcium is soluble. Although magnesium is less significant than calcium in dairy systems, it warrants more investigation. Magnesium plays numerous physiological roles in the human body and is implicated in many critical health issues such as metabolic syndrome and skeletal muscle loss. Despite its well-established significance in health, magnesium is often reported as an under-consumed nutrient. Milk and dairy products are already one of the main sources of dietary magnesium. There is an opportunity to develop milk and dairy products as efficient vehicles for supplementary dietary magnesium delivery with more research into fortification options.

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1. Introduction

Magnesium is the fifth most abundant mineral in the human body after potassium, calcium, phosphorus and sodium, but until recently it could be termed the forgotten mineral. It is the major intracellular divalent cation and plays a major role in many biochemical processes. Its functions include, protein and nucleic acid metabolism, neuromuscular transmission, bone growth and metabolism, ion channel stabilisation, energy metabolism, regulation of blood pressure, contraction of myocardial muscle cells and as a cofactor in a large number of enzymatic reactions (Volpe, 2012; Zhang, 2011).

Its significance in milk has been largely overshadowed by calcium, its more-abundant alkaline earth relative, which plays a pivotal roles in the structure of milk through its role in colloidal calcium phosphate, and hence the integrity of the casein micelle, and also in the heat stability of milk. Calcium in milk is also widely known for its nutritive value and bioavailability. As a consequence, much less has been published on magnesium than on calcium in milk and milk products. However, magnesium in milk and milk products is a major contributor of dietary magnesium and warrants more attention. This review collates much of the available information on magnesium in milk and discusses its importance in human health and disease.

2. Measurement of magnesium

2.1. Total magnesium

Total magnesium in milk can be measured instrumentally or by wet chemistry methods. Instrumental methods of analysis require an initial mineralisation procedure to eliminate organic material. This can be achieved by dry digestion by incineration (AOAC 975.03) or by a wet procedure involving, for example, a nitric acid–perchloric acid (4:1) mixture (Moreno-Torres, Navarro, Ruíz-López, Artacho, & López, 2000) or microwave-assisted combustion using nitric acid and hydrogen peroxide (Khan et al., 2014). Moreno-Torres et al. (2000) claimed that the wet method using the nitric acid–perchloric acid mixture was superior to the dry incineration method, being fast and easily controlled, and achieving complete destruction of caseins that are difficult to remove by dry incineration. Khan et al. (2014) concluded that microwave assisted digestion was suitable for milk products and that it eliminated the inaccuracy of conventional digestion methods and reduced analysis time. Following mineralisation of the sample, the magnesium, and other minerals, are commonly analysed by atomic absorption spectroscopy (AAS) (e.g., Udabage, McKinnon, & Augustin, 2000), inductively coupled plasma-atomic emission spectrometry (ICP-AES) (e.g., van Hulzen, Sprong, van der Meer, & van Arendonk, 2009) or inductively coupled plasma-optical emission spectrometry (ICP-OES) (e.g., Khan et al., 2014). Total magnesium can also be determined by ion chromatography after pre-treatment of the milk with nitric acid (Sato, Harada, & Tanaka, 1992).

There are two major traditional wet chemistry methods (Walstra & Jenness, 1984). The first involves two EDTA titrations, one using a calcium-specific indicator, such as murexide, and one using Eriochrome Black T that reacts with both calcium and magnesium. The difference between the two results is a measure of magnesium concentration. The second involves an EDTA titration of the supernatant after calcium has been precipitated as calcium oxalate.

2.2. Ionic magnesium

The ionised form of magnesium (Mg^{2+}) is regarded as the biologically active form and hence there has been considerable interest in its determination (Zhang, 2011). In blood, it is commonly performed with Mg^{2+}-selective electrodes. Dimeski, Badrick, and St John (2010) reported that these were introduced in the mid-1990s and that there were three Mg^{2+} electrodes available for clinical measurements. However, despite the fact that other ion-selective electrodes, some of which have been developed for blood analysis, e.g., Ca^{2+} electrodes (Lewis, 2011), are routinely used for analysis of milk, Mg^{2+} electrodes do not appear to have been used for this purpose. Considerable experience with these electrodes has been gained in clinical laboratories and is available for access by dairy scientists. Dimeski et al. (2010) concluded that the selectivity and specificity of Mg^{2+} electrodes in relation to Ca^{2+} were not ideal and that the interference from Ca^{2+} varies between electrodes from different suppliers. Some of the clinical Mg^{2+} analysers correct for this interference but this is more challenging for analysis of milk with its high calcium content.

One company, C-CIT Sensors AG (www.c-cit.ch), offers a Mg^{2+} ion-selective electrode that contains a replaceable Mg^{2+}-selective membrane that is claimed to be suitable for milk. The selectivity for Mg^{2+} is more than 1,000 times higher than for Na^+ or K^+ and more than 100 times higher than for Ca^{2+}. According to the manufacturer, for milk with 0.1 g L^{-1} of Mg^{2+} and 1.25 g L^{-1} of Ca^{2+}, 5–10% of the measured Mg^{2+} concentration may be attributable to Ca^{2+}. Therefore such an electrode may be suitable for milk if this level of accuracy is tolerable.

Another method for measuring Mg^{2+} is by binding it with a dye such as Magnesium 510 (Ursa BioScience LLC, www.ursabioscience.com). This dye has a strong emission spectrum with a maximum at 510 nm at an excitation wavelength of 280–415 nm. It is claimed to have high sensitivity and to react only with ionic species. While the manufacturers consider it is suitable for milk, reports of its use for this purpose have not been located.

Ionic magnesium has also been measured by the Donnan Membrane Technique (DMT) (Bijl, van Valenberg, Huppertz , & van Hooijdonk, 2013; Gao et al., 2009). A detailed description of the DMT theory and equipment was provided by Gao et al. (2009).

3. Content in milk

The average content of magnesium in cows' milk is 110 mg L^{-1} (4.6 mmol L^{-1}) although quite wide ranges have been reported: 114–130 mg L^{-1} (White & Davies, 1958); 81–268 mg L^{-1} (Cerbulis & Farrell, 1976); 97–146 mg L^{-1} (Gaucheron, 2005); 82–129 mg L^{-1} (Tsioulpas, Lewis, & Grandison, 2007); 115.9 ± 10.1(CV) mg L^{-1} (van Hulzen et al., 2009); and 114 ± 1(SD) mg L^{-1} (Bijl et al., 2013). On a dry weight bass, the magnesium content of milk (~ 1300 mg kg^{-1} for skim milk powder, Table 1) is in the mid-high range for foods. Miciński et al. (2017) reported higher levels in the first colostrum (340 and 311 mg L^{-1} for primiparous and older cows, respectively); the levels decreased to normal milk levels (120 and 100 mg L^{-1}, respectively) after 5 d. These authors commented that magnesium in colostrum has a role in activating intestinal peristalsis, which reduces the density of meconium and facilitates its expulsion. After the colostrum stage, the magnesium content shows little variation. Gaucheron (2005) reported levels in early, mid and late lactation to be 137, 120 and 130 mg L^{-1}, respectively. These were similar to the values reported earlier by White and Davies (1958), namely, 130, 118 and 12.8 mg L^{-1}, respectively. The level also appeared to be little affected by mastitic infection with the average level in milk from cows with sub-clincal mastitis reported to be 118 mg L^{-1} (White & Davies, 1958).

In a large study involving the milk from 1860 primiparous Dutch Holstein-Friesian cows from 388 herds in the Netherlands, van Hulzen et al. (2009) concluded that the variation in genetic effects for magnesium (as well as calcium and phosphorus) concentration was much greater than the variation in herd effects. This implies that there are better prospects for altering the levels of these minerals by selective breeding than by nutritional manipulation.

In another large Dutch study, bulk milk samples were collected weekly from dairy plants in 20 regions throughout The Netherlands and then mixed to give a representative weekly sample. From this study, which was conducted over one year, Bijl et al. (2013) were able to compare the levels of magnesium and other minerals found in their study with levels found 50–75 y earlier in The Netherlands. They found that the magnesium, calcium and phosphorus contents had increased by 7.2, 12.4 and 9.6% in line with a similar increase in protein content. The authors found that the content of each of these minerals had a significant positive correlation with protein content which was largely due to their association in the casein micelle.

Goats' milk contains a similar magnesium concentration to cows' milk (mean, 122 mg L^{-1}; range 110–144 mg L^{-1}) while ewes milk contains a higher concentration (mean, 193 mg L^{-1}; range 175–212 mg L^{-1}) (de la Fuente, Olano, & Juárez, 1997). Dorea (2000) reviewed several reports of magnesium in human milk and found a range of 15 to 61 mg L^{-1}, with 75% being less than 35 mg L^{-1}. Hence the concentrations in the milk of cows, goats and ewes are much higher than that in human milk.

4. Distribution between casein micelles and serum in milk and milk products

The distributions of magnesium and calcium in cows' milk, various milk products and milk fractions are given in Tables 1 and 2. Two major differences are apparent: the total magnesium contents are all much lower than the total calcium levels and the distribution between the serum and colloidal phases of milk are different. A large proportion (~ 2/3) of magnesium is in the serum fraction (Bilj et al. 2013; Gaucheron, 2005; Pyne, 1962; Udabage et al., 2000; White & Davies, 1958). This proportion is remarkably consistent between the reports listed; it even holds for milks with added magnesium sulphate (Abdulghani, Ali, Prakash, & Deeth, 2015). A similarly large proportion of calcium is in the colloidal fraction, associated with the casein micelle. Goats' milk and ewes' milk have been reported to have ~66% and ~56% soluble magnesium, respectively (de la Fuente et al., 1997).

The different distribution between the serum and colloidal phases explains the large difference between calcium and magnesium in products based on casein such as cheese. Almost all (~ 99%) of the magnesium and calcium is located in the skim milk. The low percentage associated with the fat is reflected in the very low contents in butter (Table 1).

4.1. Association with the casein micelle and colloidal calcium phosphate

According to Cashman (2011), about half (~ 20 mg L^{-1}) of the magnesium in the colloidal fraction of cows' milk is associated with the colloidal calcium phosphate (CCP) and about half (~ 20 mg L^{-1}) is bound to casein phosphoserine residues; the corresponding figures for calcium in the colloidal fraction are 75% (~600 mg L^{-1}) as CCP and 25% (~200 mg L^{-1}) attached to phosphoserine residues. Dalgleish and Law (1989) reported the effect of pH reduction on the distribution of magnesium in milk. They found a reduction in micellar magnesium with reduced pH in parallel with the effect on calcium. Micellar magnesium decreased from 1.3 mmol L^{-1} at pH 6.7 to 0.2 mmol L^{-1} at pH 4.9. Since no inorganic phosphate remained in the micelle at pH 4.9, it was suggested that the remaining magnesium may be bound to non-phosphorylated caseins. De la Fuente, Montes, Guerreroa, and Juárez

(2003) investigated the distribution of magnesium between the sedimentable (casein micelle-associated) and the non-sedimentable (soluble) fractions in yoghurt and found that 88–97% was soluble (note that at the pH of yoghurt, ~4.5, all minerals associated with CCP in the casein micelle are solubilised). Somewhat surprisingly, this was lower than that found for calcium of 96.7–99.1%, in spite of the fact that, in milk, a much higher proportion of magnesium than calcium is soluble. These authors suggested that more magnesium than calcium is bound to non-phosphorylated binding sites on the caseins.

The low proportion of magnesium found in the casein micelles may be at least partially attributable to its low affinity for inorganic phosphate and citrate in CCP. This is supported by the results obtained by adding various salts to isolated casein micelles or ultrafiltrate. Philippe, Le Graët, and Gaucheron (2005) studied the effect of adding salts of five different cations, Fe^{3+}, Zn^{2+}, Ca^{2+}, Cu^{2+} and Mg^{2+}, to dispersions of isolated casein micelles. The amount of each cation which was associated with the casein micelles following ultrafiltration was measured. Of the five cations, Mg^{2+} showed the lowest percentage (25–30%) associated with the micelles and Fe^{3+} showed the highest (98–99%). Philippe et al. (2005) also added each of the five salts to milk ultrafiltrates and measured the amounts of each cation precipitated as insoluble salts. The order of precipitate formation was $Fe^{3+} > Ca^{2+} > Zn^{2+} > Cu^{2+} > Mg^{2+}$. Precipitation indicates association of the cations with inorganic anions such as phosphate and citrate forming insoluble salts. About half of the magnesium added at 9.6 mmol kg^{-1} precipitated. Calcium, zinc and iron added at 7.4–9.56 mmol kg^{-1} showed much higher precipitation levels. The association of magnesium appeared to be mostly with phosphate as the citrate levels remained almost constant with added magnesium. The authors found a reasonable correlation between the amounts of the cations precipitated as phosphate and citrate and the stability constants of the cation–anion combinations. For example, for inorganic phosphate, the stability constants for Fe^{3+} and Mg^{2+} were 3.61 and 0.6 , respectively, and for citrate they were 11.2 and 2.8, respectively.

4.2. Magnesium in milk serum

In milk serum, the concentrations of magnesium citrate and magnesium hydrogen phosphate are 2.0 and 0.3 mmol L^{-1}, respectively; the corresponding values for calcium are 6.9 and 0.6 mmol L^{-1}, respectively (Neville, 2005). The higher concentration of magnesium citrate than magnesium hydrogen phosphate differs from the results of Phillipe et al. (2005) that showed greater association of magnesium with inorganic phosphate than citrate when a soluble magnesium salt was added to milk ultrafiltrate.

A larger percentage of magnesium than calcium in milk is present as the free or ionic form, although the absolute concentration of ionic magnesium is much lower than that of ionic calcium. According to Christianson, Jenness, and Coulter (1954), ionic magnesium is 0.82–0.85 mmol L^{-1} which is similar to 0.81 mmol L^{-1} calculated for milk diffusate by Holt, Dalgeish, and Jenness (1981), a value now generally accepted. However, Bijl et al. (2013), using the Donnan Membrane Technique, reported a somewhat lower Mg^{2+} value of 0.61 mmol L^{-1}. Gao et al. (2009) also used this technique to analyse reconstituted skim milk (200 g skim milk powder dissolved in 1800 g deionised water) and found the Mg^{2+} concentration to be 0.58 mmol L^{-1}. The concentration of the ionic form of calcium in cows' milk is ~ 2 mmol L^{-1} (Lewis, 2011).

Another difference between magnesium and calcium in the serum phase is that some calcium (about 0.5 mmol L^{-1} in milk) is bound to α-lactalbumin (α-La), whereas no magnesium is bound to this protein. Calcium is bound in a one atom per molecule stoichiometry (Hiroaka, Segawa, Kuwajima, Sugai, & Murai, 1980).

4.3. Effect of heating on the distribution of magnesium in milk

Thermal processing followed by cooling has little effect on the distribution of magnesium between the major fractions of milk (Abdulghani et al., 2015). However, when milk was heated to 90 °C, a decrease (~ 18%) occurred in the concentration of magnesium in the soluble phase, at that temperature. This was shown by analysing the permeate from ultrafiltration performed at this temperature rather than on the soluble phase obtained after cooling the heated milks (Pouliot, Boulet, & Paquin, 1989a,b,c; Holt 1995). The decrease in soluble calcium under the same conditions was much greater, ~ 33%. The decrease in soluble minerals is due to their migration into the calcium phosphate microgranules as evidenced by the increase in the size of these particles. It appears to occur in two phases, whereby most of the redistribution occurs rapidly, in less than one minute, in the first phase and a further smaller decrease occurs over several minutes, up to 2 h, in a second phase. According to Holt (1995), the difference in redistribution behaviour of magnesium and calcium suggests that magnesium is associated with the surface of the calcium phosphate microgranule while calcium is associated with the bulk of this particle. On cooling heated milk, the redistribution of magnesium and calcium is almost totally reversible (Pouliot et al., 1989b), which explains why other authors have observed little change in distribution after heating (e.g., Abdulghani et al., 2015). Similarly, Le Ray et al. (1998) found no change in mineral distribution between casein micelles and the serum of a casein micelle suspension when heated to 95 °C for up to 30 min.

On heat treatment of skim milk concentrate to ~ 130 °C (heated in a glass tube in an oil bath at 135 °C for 45 s), both magnesium and calcium in the soluble phase decreased (by 15 and 6% respectively). However, on storage at 30 °C for up to 120 d, the soluble magnesium increased by ~ 22% while the soluble calcium decreased by ~25%. Concomitantly, soluble casein increased approximately three-fold to account for about 2/3 of total casein after 120 d (Aoki & Imamura, 1974). These results further reflect the different associations of calcium and magnesium with the caseins and CCP.

5. Interactions with proteins

5.1. Interaction of magnesium with caseins

It has long been known that caseins can be precipitated by magnesium (or calcium or acid) from milk (O'Mahony & Fox, 2016). Although little magnesium is naturally associated with proteins in milk, added magnesium ions can interact with casein and induce formation of a gel or a coagulum when milk is heated to ~ 70 °C in much the same way as do calcium ions (Ramasubramanian, 2013; Ramasubramanian, D'Arcy, & Deeth, 2012; Ramasubramanian, D'Arcy, Deeth, & Oh, 2014). The strength of the gel or coagulum is strongly influenced by the prior heat treatment; for example, treatment at 90 °C for 60 min leads to high-strength gels or coagulums while UHT treatment (140 °C for 4 s) leads to very weak gels or coagulums. Gels form in heated milk with 12.5–20 mmol L^{-1} added magnesium chloride (Lim, 2015) and coagulums form at >20 mmol L^{-1} (Ramasubramanian, 2013). While magnesium ions have a similar destabilising effect to calcium ions on the casein in milk during heating, they have "a much inferior role" in rennet coagulation (Pyne, 1962).

Cuomo, Ceglie, and Lopez (2011) investigated the precipitation of sodium caseinate (4 mg mL^{-1} in 0.1 M NaCl) by magnesium and calcium ions. Magnesium at 2.5 mmol L^{-1} did not cause casein precipitation from the caseinate solution heated to 90 °C, at 5 mmol L^{-1} it caused precipitation at ≥~ 70 °C, at 7.5 mmol L^{-1} precipitation occurred at ≥~ 50 °C, and at

10 mmol L^{-1} precipitation occurred at ≥~ 40 °C. Precipitation occurred more readily with calcium than with magnesium. For example, 5 mmol L^{-1} calcium precipitated caseinate at ≥~ 60 °C compared with ≥~ 70 °C for magnesium. Interestingly, a combination of 2.5 mmol L^{-1} calcium plus 2.5 mmol L^{-1} magnesium caused precipitation at ≥~ 65 °C. The interaction of calcium with casein was influenced by both temperature and solvent (the authors compared precipitation in both H_2O and D_2O) but the interaction with magnesium was influenced by temperature only. They concluded that the two ions have different binding sites on the casein: phosphoserine for calcium, and glutamic and aspartic acids for magnesium. They suggested that this enabled the calcium and magnesium to act cooperatively and the presence of calcium aids the binding of magnesium by making more sites available; this may explain the synergistic effect of magnesium and calcium ions when both are added at 2.5 mmol L^{-1}.

Le Ray et al. (1998) added 19 mmol kg^{-1} calcium chloride and magnesium chloride to dispersions of casein micelles and found that both salts reduced the pH of the dispersion with the effect of the calcium being greater than that of magnesium, calcium caused a decrease in the micellar water content (by ~8%) but magnesium made no significant change. The authors suggested the difference could be attributed to the different hydrated ionic radii (Ca^{2+} = 0.412 nm, Mg^{2+} = 0.428 nm and electronegativities (calcium = 1.2; magnesium = 1 on the Pauling scale). Addition of magnesium ions caused a partial displacement of the calcium in the casein micelles such that the concentration of calcium and magnesium ions in the centrifugation supernatant was almost equal to that of the added magnesium. On heating to 90 °C for 30 min, and adding magnesium chloride at 2.6, 9.3 and 19.3 mmol kg^{-1}, the proportion of protein precipitated was 33, 95, and 96%; calcium chloride addition at 10.5, 13.7 and 19.0 mmol kg^{-1} resulted in ≥ 95% precipitated.

5.2. Interaction of magnesium with whey proteins

The association with α-La accounts for about 1.5% of the calcium in milk but a negligible percentage of magnesium, although the latter can bind to α-La. Magnesium binds weakly to α-La in a molar ratio of 2:1 with two association constants at 20°C of 2×10^2 and 2×10^3 M^{-1}. These are much lower than the association constant for calcium of 3×10^8 M^{-1}, which explains the negligible amount of magnesium bound to α-La in milk. One magnesium atom binds to the calcium-binding site that is formed by the carboxylic groups of three aspartate residues (82, 87 and 88) and two carbonyl groups of the peptide backbone (79 and 84), and the other magnesium binds to a secondary binding site (Permyakov & Berliner, 2000). Permiakov, Morozova, Iarmolenko, and Burshteĭn (1982) earlier reported that magnesium ions in millimolar concentrations have little effect on the association of calcium ions with α-La, which led them to suggest that calcium and magnesium ions bind to different sites on the protein. It appears now that one of the magnesium binding sites is the same as the calcium binding site but that the binding of magnesium is much weaker than that of calcium.

When bovine serum albumin (BSA) dispersions in 1 M NaCl containing 5 mmol L^{-1} Mg^{2+} (as MgSO_4), were heated at 90 °C for 15 min, a gel with a compact matrix resulted that was stronger that the control gel without Mg^{2+} and gels made with Cu^{2+}, Fe^{2+} and Zn^{2+}. This was attributed to magnesium binding to the denatured protein forming small dense aggregates of 0.05 µm diameter with small void spaces (length of maximum void space of 0.7 µm); by contrast, the other three metal ions formed larger clustered aggregates of 0.1–0.5 µm with maximum void space lengths of 7.6–40 µm. The corresponding data for the control gel without added metal ions were 0.1 and 3.2 µm respectively (Haque & Aryana, 2002). The effect of calcium was not included in this study.

The effects of magnesium or calcium ions on heat-induced denaturation (as measured by protein removed by centrifugation at the heating pH) and aggregation (as measured by protein removed by centrifugation at pH 4.6) of whey proteins is dependent on pH (Varunsatian, Watanabe, Hayakawa, & Nakamura, 1983). When WPC was heated at 80 °C for 15 min without added metal ions, denaturation and aggregation of WPC were maximised (> 90%) at the isoelectric point (~5.5); at pH ≤ 4.5, both aggregation and denaturation were < 80% while at pH values of 6.5-9.5, aggregation was ≤ 90% but denaturation was 30-80%. When magnesium or calcium ions were added before heating at pH values of 5.5–9.5, both denaturation and aggregation were > 90%. At pH values ≤ 4.6, magnesium and calcium ions had no effect on the extents of denaturation or aggregation. The effect of magnesium on the denaturation and aggregation was less than that of calcium. For example, heating WPC at pH 8 at 70 °C and 75 °C caused aggregation of ~ 55 and 85%, respectively, in the presence of Mg^{2+} but ~75 and 90%, respectively, in the presence of Ca^{2+}. Consistent with this is the different denaturation temperatures for the WPC proteins in the presence of: no metals (75.2 °C), Mg^{2+} (73.5 °C) and Ca^{2+} (71.5 °C) (Varunsatian et al., 1983).

Cerbulis and Farrell (1986) reported the precipitation of whey proteins from cheese whey by magnesium acetate (4%, w/v); 70% was precipitated at pH 6.7 and ~100% at pH 10.5. Magnesium acetate was more effective than calcium hydroxide but a mixture of 1% magnesium acetate and 1% calcium hydroxide (pH 10.9) precipitated 98%; 2% magnesium acetate and NaOH (to adjust the pH 9.9) precipitated 95.5% of the whey proteins.

Magnesium chloride, along with calcium chloride and ferrous chloride, can induce formation of whey protein gels through a cold gelation process (da Silva & Delgado, 2009; Tomczyńska-Mleko & Mleko, 2014). Gelation is achieved by salt-induced aggregation of the whey proteins that are unfolded by a pre-heat process at a pH and ionic strength that maintain high electrostatic repulsion forces between the proteins and prevent aggregation. Added magnesium, calcium or iron salts decrease the electrostatic repulsion between the protein molecules and form salt bridges between negatively charged groups on the proteins. Da Silva and Delgado (2009) used a pre-heat process of WPI dispersions of 75 °C for 20 min. at pH 7.0. From trials with mixing solutions of various concentrations of magnesium chloride and WPI at 25 °C, they constructed a phase diagram of Mg^{2+} concentration versus WPI concentration which contained areas for each of three phases, “sol”, “sol-gel” and “gel”. The “gel” area included all points > about 10 mmol L^{-1} Mg^{2+} and 3% of WPI protein. Above 15 mmol L^{-1} magnesium and 3.5 wt % protein, the cold-set gel exhibited no syneresis. From penetrometer studies, the gel formed with 7.5% WPI and ~ 30 mmol L^{-1} Mg^{2+} had a Young’s modulus of ~ 50,000 Pa. Tomczyńska-Mleko and Mleko (2014) used pre-heat conditions of 80 °C for 30 min at pH 6.68 and found that strong cold gels were formed with 7% WPI at 30 mmol L^{-1} Mg^{2+}, 20 mmol L^{-1} Ca^{2+} or 10 mmol L^{-1} Zn^{2+}. The gels formed with 30 mmol L^{-1} Mg^{2+} had a G′ at 10 Hz of ~1800 Pa. They also produced a corresponding aerated gel which had a G′ value of ~ 1500 Pa. These authors observed a slow release of the magnesium from the gels in simulated gastric conditions and suggested the gels could be used for supplementation of the human body with magnesium (Tomczyńska-Mleko & Mleko, 2014).

5.3. Alkaline phosphatase

Magnesium is involved in many enzymatic reactions. According to Volpe (2012) there are more than 300 such reactions requiring it in the human body. In milk, magnesium activates alkaline phosphatase and also strongly enhances reactivation of alkaline phosphatase previously inactivated by heat. Murthy, Cox, and Kaylor (1976) reported conditions for optimal reactivation of alkaline phosphatase which included 64 mmol L^{-1} Mg^{2+}.

Furthermore, magnesium ions also increase the activity of the reactivated enzyme ~15-fold while they activate the native enzyme only 2-fold. Methods based on this difference in activation are used to distinguish between native and reactivated alkaline phosphatase. This is important because inactivation of the native enzyme is used to determine the adequacy of pasteurisation of milk.

6. Magnesium supplementation and fortification/enrichment of milk

In a mineral supplement survey of 8,860 adults (≥ 19 y) in the USA over the period 2003–2006, Bailey, Fulgoni, Keast, and Dwyer (2011) found that the average daily magnesium intake of male non-users of supplements was 268 mg, male supplement users was 449 mg, female non-users was 234 and female users was 387 mg. They estimated that the percentages of consumers with inadequate intakes of magnesium to meet the Estimated Average Requirement were 63% of male non-users of supplements, 22% of male supplement users, 69% of female non-users and 19% of female users.

Magnesium is a necessary mineral for a healthy body which contains approximately 25 g of magnesium of which 50–60% resides in bones (Volpe, 2012). USDA (2009) estimated that 57% of the US population may have an inadequate intake of magnesium. Therefore there is interest in enriching some foods, including water, with magnesium which may be appropriate for some people (Abrams & Atkinson, 2003; Cohen et al., 2002).

The increasing worldwide production of ultra-high temperature (UHT)-processed milk (Chavan, Chavan, Khedkar, & Jana, 2011), its long shelf-life at room temperature and its relatively low natural content of magnesium (110 mg L^{-1}, a serving of 250 mL contains < 10% of the adult RDI) makes it a suitable food product for fortification. Abdulghani et al. (2015) fortified UHT milk with up to 320 mg L^{-1} magnesium (100% of recommended daily intake, RDI) with magnesium sulphate. Because magnesium ions above a certain concentration destabilise milk proteins and cause fouling when milk is heated in heat exchangers, trisodium citrate (5 mmol L^{-1}) was added to prevent this occurring. Sensory evaluation of the fortified milks showed that addition to 75% of RDI (190 mg L^{-1} added magnesium) caused a change in taste but no change could be detected with addition to 50% of RDI (60 mg L^{-1} added magnesium). Tateo, Bononi, Testolin, Ybarra, and Fumagalli (1997) also used trisodium citrate (8–9 mmol L^{-1}) when preparing fortified milk containing 58 mg L^{-1} (2.5 mmol L^{-1}) added magnesium lactate and 560 mg L^{-1} (14 mmol L^{-1}) added calcium lactate. Commercial magnesium-fortified UHT milk has also been reported (Mendoza, Olano, & Villamiel, 2005; Tateo et al., 1997). One commercial milk sample analysed by Tateo et al. (1997) contained a total of 146 mg L^{-1} (6.3 mmol L^{-1}).

7. Absorption of magnesium from dairy food

Magnesium is known to be absorbed in the duodenum and ileum in humans (Greger, Smith, & Snedeker, 1981). Digestion leads to dissociation of magnesium from the digestate, hence magnesium is released into the system as a soluble cation. Lindberg, Zobitz, Poindexter, and Pak (1990) suggested that magnesium salts with the greatest aqueous solubility resulted in the highest bioavailability of magnesium. The absorption of magnesium is considered to be by both passive (diffusion) and active transport (Harris, 2014). Magnesium homeostasis in the human body is the net effect of the intestinal absorption and renal excretion of magnesium ions (Vormann, 2012).

Unlike calcium, there have been a limited number of human studies of the bioavailability of magnesium. There is some indication that the absorption of dietary magnesium may decrease with ageing although a comprehensive study has not been reported to date (Durlach et al., 1993; Verhas et al., 2002). A study in adult men showed the mean magnesium absorption rate of 59% from mineral water (Verhas et al., 2002). The reported absorption rates of magnesium from food vary widely depending on the source, ranging from 10 to 75% (Schwartz, Spencer, & Welsh, 1984; Sojka et al., 1997; Verhas et al., 2002). Anti-nutrients in plant-based food such as phytate and oxalate that are known to influence the absorption of other minerals such as calcium, iron and zinc also influence the absorption of magnesium. Unleavened bread has been implicated as a source of such anti-nutrients. The presence of phytate in pea flour showed an inhibitory effect on magnesium absorption in rats by forming insoluble complexes with the mineral; the high levels of insoluble dietary fibre in pea flour may also hinder the absorption of magnesium by a solvent drag mechanism (Urbano et al., 2007).

Lonnerdal, Yuen, Glazier, and Litov (1993) reported that in suckling rat pups, there was no significant difference between the magnesium absorption from human milk, cows' milk and infant formula, despite the moderate variations in the food sources. It was proposed that magnesium from the different infant food sources was similarly absorbed and retained as it exists predominantly as low-molecular-weight compounds (Lonnerdal et al., 1993). On the other hand, Delisle, Amiot, and Dore (1995) investigated the availability of magnesium and calcium in dairy products to rats. The apparent absorption of magnesium from cheese was found to be lower than that from yoghurt, skim milk powder, skim milk and evaporated milk. The authors attributed the lower absorption from cheese to its lower lactose content compared with the other dairy foods, referencing the positive correlation between intestinal absorption of magnesium and calcium, and the dietary lactose content.

Lactose has a stimulant effect on net absorption of magnesium along with calcium and manganese in human infants (Ziegler & Fomon, 1983). Lactose may also aid apparent absorption and/or retention of magnesium in rats (Greger, Gutkowski, & Khazen, 1989; Heijnen, Brink, Lemmens, & Beynen, 1993). Heijnen et al. (1993) proposed that the stimulant effect of lactose is caused by a lowering of ileal pH. However, the study by Brink, Vanberesteijn, Dekker, and Beynen (1993) implied that lactose intake does not influence the absorption of magnesium and calcium in healthy, lactose-tolerant adults, as hydrolysing lactose did not affect the absorption of these minerals.

Lactulose is an indigestible oligosaccharide that is present in low concentrations in heat-treated milk. Seki et al. (2007) demonstrated that lactulose improved the absorption of magnesium as well as calcium in adult males. A similar enhancing effect of lactulose on magnesium absorption was reported in rats (Heijnen et al., 1993). However, a high dietary intake of lactulose is not advisable due to it laxative effect.

The effect of other minerals on the absorption of magnesium has been examined by various researchers; however, there is no coherent evidence that modest rises in calcium, iron or manganese intakes influence magnesium balance (Abrams & Atkinson, 2003; Andon, Ilich, Tzagournis, & Matkovic, 1996; Lonnerdal, 1995; Sojka et al., 1997). Mahalko, Sandstead, Johnson, and Milne (1983) reported that apparent mineral absorption and balance were not affected by a modest increase in dietary protein intake (from 65 g to 94 g protein d^{-1}). On the other hand, the types of protein in the diet may influence the absorption of magnesium. For instance, Ishikawa, Tamaki, Arihara, and Itoh (2007) indicated that egg yolk protein reduced calcium and magnesium absorption compared to casein and soy protein. In terms of milk protein fractions, β-casein was shown to improve magnesium absorption better than the other fractions (Pantako, Passos, Desrosiers, & Amiot, 1992).

8. Significance of magnesium in health

The USA recommended daily intake (RDI) of magnesium is 400 mg d^{-1} for adult males between 19 and 30 y and that of adult females is 310 mg d^{-1}. For adults over 30 y, the RDI values increase slightly to 420 mg d^{-1} and 320 mg d^{-1} for males and females, respectively. The European Food Safety Authority (EFSA, 2015) uses Adequate Intake (AI) values which are set at 350 mg d^{-1} for men and 300 mg d^{-1} for women. Dietary reference values are very similar amongst various countries, generally between 300 and 400 mg d^{-1}. The average need for magnesium is dependent on a number of factors, including gender, age, body habitus, and individual variation in intestinal and renal reabsorption, and excretion (Glasdam, Glasdam, & Peters, 2016). In individuals without renal failure, oral magnesium supplementation cannot result in serum concentration that could be harmful (Vormann, 2012).

Although magnesium is widely distributed in both plant and animal foods, the Dietary Guidelines for Americans 2015–2020 listed magnesium as one of the under-consumed nutrients along with calcium as the surveyed intake level did not meet the estimated average requirement. The National Diet and Nutrition Survey of 2014 also reported a similar observation in the UK population that a substantial proportion of adults aged 19 y and over had magnesium intakes below the Lower Reference Nutrient Intake (LRNI: the level of intake considered likely to be sufficient to meet the needs of only the small number of people who have low requirements, 2.5% of the population. The majority need more.). The importance of milk and dairy products in meeting the daily magnesium intake requirement is often overshadowed by the strong emphasis placed on being a significant food group for calcium. Milk and dairy products are, in fact, one of the main dietary sources of magnesium particularly for children, contributing approximately 10–30% of the total magnesium intake (EFSA, 2015).

A low level of dietary magnesium intake has been implicated in an array of health issues in the current literature, including metabolic syndrome, skeletal muscle loss, kidney function decline and depression (Bain et al., 2015; Rebholz et al., 2016; Welch et al, 2016; Yary et al., 2016; Zhang et al., 2016). The diversity of the health issues associated with magnesium reflects the multitude of roles magnesium plays in the human body. As the second most abundant cation in the intracellular compartment after potassium, magnesium activates many enzyme systems, including those involved in energy metabolism and functions as an essential regulator of calcium flux and the intracellular actions of calcium (Glasdam et al., 2016; Sales & Pedrosa, 2006). The syntheses of DNA, RNA and protein are also dependent on magnesium (Vormann, 2012).

Recent meta-analyses signal the importance of magnesium intake in the likelihood of developing metabolic syndrome as an inverse association between magnesium intake and metabolic syndrome has been found (La et al., 2016; McKeown, Jacques, Zhang, Juan, & Sahyoun, 2008; Sarrafzadegan, Khosravi-Boroujeni, Lotfizadeh, Pourmogaddas, & Salehi-Abargouei, 2016). In particular, the link between magnesium and hypertension has been long considered by many researchers. Zhang et al. (2016) reported an effect of magnesium supplementation on lowering blood pressure in adults and suggested the possibility of recommending increased magnesium intake for the prevention of hypertension. Bain et al. (2015) showed that lower dietary magnesium intake was related to elevated blood pressure and higher stroke risk in a UK representative population. A similar conclusion was drawn by King, Mainous, Geesey, & Woolson (2005) in a general USA population where lower magnesium in the diet was associated with elevated C-reactive protein levels which indicate increased risk of cardiovascular disease events.

Nielsen, Milne, Klevay, Gallagher, and Johnson (2007) reported that magnesium deficiency induced by feeding a low-magnesium diet led to impaired glucose tolerance, as well as heart rhythm, cholesterol and oxidative metabolism changes in post-menopausal women. It is worth noting that the diet used by the subjects in the Neilsen et al. (2007) study was composed of ordinary western food, which would not be considered unusual except that it was designed to provide only 101 mg magnesium per 2000 kcal for the research purposes.

Magnesium has also been evaluated for its potential in improving insulin sensitivity and preventing diabetes. A meta-analysis by Fang et al. (2016) concluded that there is a significant linear dose-response relationship between dietary magnesium intake and the risk of Type 2 diabetes, such that an additional daily intake of 100 mg magnesium was associated with an 8–13% reduction in risk of Type 2 diabetes. Hypomagnesaemia is known to be prevalent in Type 2 diabetes patients although the underlying reasons have not been clearly identified (Kurstjens et al., 2017).

Magnesium intake may be relevant in healthy ageing. It is inversely correlated with the occurrence of the metabolic syndrome in older adults (McKeown et al., 2008). Ageing itself is, in fact, a major risk factor for magnesium deficit. Bone is the main storage organ of magnesium in the body. As the bone mass decreases with age, the total magnesium level in the body also decreases (Barbagallo, Belvedere, & Dominguez, 2009). Barbagallo et al. (2009) suggested that the primary magnesium deficit with ageing may be caused by inadequate magnesium intake, lower efficiency of magnesium absorption and increased urinary excretion associated with reduction in kidney function. Magnesium is also directly involved in muscle physiology. Dominguez et al. (2006) demonstrated that serum magnesium concentrations were significantly linked to indexes of muscle performance, including grip strength, lower-leg muscle power, knee extension torque, and ankle extension strength in older adults. A cross-sectional study of women by Welch et al. (2016) showed a positive association of dietary magnesium with indices of skeletal muscle mass and leg explosive power, indicating dietary magnesium could be further investigated for its function in maintaining skeletal muscle mass and power in women. Loss of skeletal muscle mass and strength due to ageing are risk factors for diseases such as sarcopenia and osteoporosis, which draws attention to magnesium status of older adults (Welch et al., 2016). Despite the important roles magnesium may play in ageing health, ter Borg et al. (2015) reported that the magnesium intake of community-dwelling older adults was inadequate along with their calcium and other micronutrient intakes.

9. Conclusion

It is clear that maintaining the optimum magnesium balance is important in human health. Magnesium-fortified milk and dairy products may contribute towards overcoming reported magnesium deficiencies and address specific health needs. With a better understanding of magnesium in the dairy system, there is potential for milk and dairy products to be developed to deliver increased levels of bioavailable magnesium, as well as calcium.

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Table 1

Comparison of magnesium with calcium contents in milk and milk products and milk fractions. [a]

Product	Magnesium	Calcium
Colostrum (d 1)	400	2600
Milk	110	1180
Cream (35–48% fat)	60	580
Skim milk powder	1300	12800
Evaporated milk (whole)	290	2900
Condensed milk (whole)	290	2900
Butter	20	180
Cheese - Cheddar	290	7390
Cheese - cottage	130	1270
Yoghurt	190	2000
Dairy ice cream	120	1000

[a] Values are in mg L^{-1} or mg kg^{-1}. Sources are: Alexander and Ford (1957); Christianson, Jenness, and Coulter (1954); Cashman (2011); Lucey and Horne (2009); Marnila and Korhonen (2011); Van Kreveld and Van Minnen (1955).

Table 2

Distribution of magnesium and calcium in various fractions of milk. [a]

Milk fraction	Magnesium		Calcium		Fraction with which associated	Magnesium		Calcium	
	%	mmol L^{-1}	%	mmol L^{-1}		%	mmol L^{-1}	%	mmol L^{-1}
Fat	1		1						
Colloidal	36	1.9	66	19.4	Casein	18		50	
					Colloidal calcium phosphate	18		16	
Serum	64		34		Magnesium or calcium citrate	40	2	23	6.9
					Magnesium or calcium phosphate	7	0.3	2	0.6
					Ionic or free form	16	0.8	7	2
					Bound to α-lactalbumin	0	0	1.5	0.5

[a] Percentages are given as of total. Sources: Cashman (2011); Lucy and Horne (2009); Neville (2005).