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Compounds Influencing Magnesium Absorption

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Abstract

Magnesium (Mg^{2+}) is the fourth most abundant cation in the body and the second most common at the Intracellular Level (IC). In humans, it is involved in the activity of hundreds of enzymes, covering approximately 80% of metabolic functions. Homeostasis is achieved by a balance between ingestion, excretion, and reservoir. According to data from Health and Nutrition Organizations, an important percentage of individuals consume less than the Dietary Reference Intake (DRI) of magnesium from food. In the intestine, there are several inhibitors and enhancers of magnesium absorption. This includes physicochemical and dietary factors. This narrative review aims to evaluate the compounds influencing Mg^{2+} absorption. These factors can be considered when determining Dietary Reference Intakes (DRIs) for the population to prevent deficiency and non-communicable diseases. The recommendations aim to increase fruit and vegetable consumption, as they are mineral-rich and alkalinizing foods.

Keywords: Magnesium; Magnesium absorption; Magnesium intake; Dietary factors

Introduction

Magnesium (Mg^{2+}) is the fourth most abundant cation in the body and the second most common at the Intracellular Level (IC)[1]. In humans, it is involved in the activity of hundreds of enzymes, covering approximately 80% of metabolic functions [2]. The fine regulation of serum Mg^{2+} concentrations is maintained through a balance of intake, intestinal absorption, renal excretion, and bone reserves. In intestine, Mg^{2+} homeostasis is poorly regulated and primarily depends on Mg^{2+} intake [3]. Mg^{2+} is absorbed throughout the intestine by mechanisms acting at the paracellular and transcellular level [4]. Several factors can influence Mg^{2+} intake, particularly bioavailability and its content in food [5]. This includes physicochemical (amount of Mg^{2+} ingested, transit time, pH, and solubility) and dietary factors (fermentable carbohydrates, polyphenols, phytates, oxalic acid, proteins, lipids, minerals and probiotics). Low Mg^{2+} content in soils, food, and modern Western dietary habits is prevalent today, resulting in insufficient Mg^{2+} intake [6] and probably compromised status. According to data from Health and Nutrition Organizations [7-11], an important percentage of individuals consume less than the Dietary Reference Intake (DRI) of Mg^{2+} from food. This narrative review aims to evaluate Compounds Influencing Mg^{2+} Absorption, which are essential for planning a healthy diet and determining DRIs to prevent deficiency and non-communicable diseases.

Magnesium Homeostasis

Under physiological conditions, serum Mg^{2+} levels are maintained at constant values, ranging from 0.7 to 1.1 mM Mg^{2+} homeostasis is maintained through the coordinated actions of intake, intestinal absorption, renal excretion, and storage in bone [3].

Magnesium homeostasis in the intestine

In the gut, Mg^{2+} homeostasis is poorly regulated and primarily depends on Mg^{2+} intake [3]. In the proximal intestine, Mg^{2+} absorption occurs through both passive (paracellular) and active (transcellular) mechanisms [4]. Passive Mg^{2+} absorption accounts for 90% of Mg^{2+} uptake. These paracellular movements are facilitated by Claudins 2, 7 and 12 in the small intestine [12] and Claudins 16 and 19 in the large intestine [4]. Active (transcellular) mechanisms are mediated by the Transient Receptor Melastatin 6 (TRPM6) and the ubiquitously expressed Transient Receptor Melastatin 7 (TRPM7) channels. TRPM6 channels are found in the small intestine (duodenum, jejunum, and ileum) [4], as well as in the distal parts of the intestine. However, fine absorption primarily occurs in the distal parts of the intestine (cecum and colon), mediated by the TRPM6 and TRPM7 channels on the luminal side of the enterocyte, the Cyclin M family proteins (CNNM4) on the basolateral side, and dependent on the activity of Na^+/K^+ ATPase. This segment is crucial when Mg^{2+} intake is low, as TRPM6 expression is upregulated [12].

Factors Affecting Magnesium Absorption in the Intestine

In the intestine, physicochemical and nutritional factors influence the absorption of Mg^{2+} [13].

Physicochemical Factors

Include the amount of Mg^{2+} ingested, transit time, pH, and solubility.

Amount of magnesium ingested

It is well known that the relative absorption of Mg^{2+} is inversely related to intake, with the amount of Mg^{2+} in the digestive tract being the primary factor controlling absorbed Mg^{2+} [13]. Intake may be affected by Mg^{2+} content in food which may be affected among others by food processing, refining [14-15] and boiling [16].

Transit Time

There is a correlation between gastrointestinal transit time and Mg^{2+} absorption, which depends on the content of the meal and how it is distributed throughout the day rather than being consumed in a single large dose. Fluid intake and dietary fibers has been demonstrated to be a significant factor in relation to transit time [17].

pH

Observations from both older and more recent studies indicate that a lower pH in the intestinal tract enhances absorption efficiency [4]. The intestinal epithelial cells can modulate their response through proton-sensing channels such as the Acid-Sensing Ion-Channel 1a (ASIC1a). Luminal protons stimulate ASIC1, which promotes Mg^{2+} absorption [18].

Solubility

For Mg2+ to be absorbed, it must be soluble. Various factors, including nutritional factors, influence its solubility and hence its absorption [13].

Dietary Factors

Include fermentable carbohydrates, polyphenols, phytates, oxalic acid, proteins, lipids, minerals and probiotics [19].

Fermentable Carbohydrates:

Dietary fiber is categorized as soluble, insoluble, fermentable, and non-fermentable. Components with high fermentability include oligosaccharides and inulin, also known as Fructo-Oligosaccharides (FOS), and polydextrose, which are considered prebiotics [20]. It is well known that they produce short-chain fatty acids (SCFA), which reduce the pH in the intestinal lumen, leading to hypertrophy of the intestinal mucosa and increasing Mg^{2+} transport through the transcellular pathway [21].

Polyphenols

There are limited studies assessing the impact of polyphenols on Mg^{2+} absorption, and varied results have been observed depending on the specific phenolic compounds involved. Some suggest that polyphenols chelate metals like iron and Mg^{2+}, reducing their bioavailability [22], while others believe polyphenols may stimulate microflora, boosting SCFA production [23] and hence stimulating Mg^{2+} absorption.

Phytates

Studies have shown that diets rich in phytates decrease the absorption of certain minerals, including Mg^{2+}. Phytates chelate Mg^{2+} , reducing its bioavailability in a dose-dependent manner [24]. Phytic acid, or myo-inositol hexaphosphate, is present in all types of seeds and is concentrated in the aleurone and germ at levels from 3%-6% [25]. As phytate carries six phosphate groups, it can bind to several cations, including Mg^{2+}, preventing its absorption [26].

Oxalic acid

It is known to impair Mg^{2+} absorption and can also affect other minerals, such as calcium [27]. When combining phytates, Mg^{2+} and OA may form sparingly soluble complex with Mg^{2+} in the intestine [14], which could reduce the bioavailability of Mg^{2+} in Mg^{2+} rich foods [28].

Proteins

Contradictory results have been observed regarding the effect of proteins on Mg^{2+} absorption [29-31]. The origin of the protein (vegetable or animal) can affect its bioavailability [30]. Rats fed soy protein have shown a decrease in Mg^{2+} absorption [32], whereas diet with casein may increase Mg^{2+} absorption [33], likely due to the high phytate content in soy protein. Human studies have indicated that high protein intake increases Mg^{2+} absorption, probably by preventing the precipitation of Ca^{2+}-Mg^{2+}-Pi complexes in the ileum [13].

Lipids

It is known that long-chain fatty acids LCFAs form insoluble soaps with Mg^{2+}, which can affect nutrient absorption [13]. However, other study [34] revealed that SCFA (acetate, butyrate, propionate) at physiological concentrations stimulate absorption in the large intestine, specifically in the distal colon.

Minerals

Sodium: There is controversy regarding the effects of dietary sodium on Mg^{2+} status. Contrary to some studies [35],

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it has been shown that a high-sodium diet does not affect Mg^{2+} excretion or transport in the DCT [36]. Sodium may also influence EC volume; a high sodium diet can cause volume expansion, leading to decreased Mg^{2+} reabsorption, while volume contraction can increase Mg^{2+} reabsorption [37].

Calcium: Increasing dietary calcium has been shown to significantly decrease Mg2+ absorption. In recent years, calcium intake has increased by 2 to 2.5 times compared to Mg2+ intake, resulting in a Ca2+/Mg2+ ratio greater than 3, whereas optimal values are approximately a Ca2+/Mg2+ ratio of 2. An increase in the Ca2+/Mg2+ ratio, coupled with vitamin D supplementation and suboptimal Mg2+ intake, may result in pathological implications [38] such as those related with hypomagnesemia.

Phosphate: The interaction between phosphate and Mg2+ in the intestine is complex and depends on various factors, including age, luminal contents, and the intake of both minerals [13]. In human studies, an increase in dietary phosphate has been shown to decrease Mg2+ absorption because Mg2+ forms insoluble salts when complexed with phosphates [39].

Probiotics:

Probiotics can influence microbiota by inhibiting pathogenic bacteria, competing for nutrients and binding sites, and producing beneficial metabolites [40-41]. It has been demonstrated that probiotics such as C4 L. plantarum [42] and other strains [43] modulates Mg^{2+} status and influence microbiome. Currently, it is unknown how the small intestinal microbiome may affect intestinal Mg^{2+} absorption, but acidification by enterobacteria and changes in the absorptive surface in the gut may be related. Interestingly, dietary Mg2+ deficiency in C57BL/6 mice has been shown to alter gut microbiota, which in turn leads to depressive behavior [44].

Conclusion

According to data from different studies [7-11], an important percentage of individuals consume less than the Dietary Reference Intake (DRI) of Mg^{2+} from food. Low Mg^{2+} content in soils, food, and modern Western dietary habits [45] is prevalent today, often resulting in insufficient vegetables and fruits intake. Mg^{2+} deficiency can lead to the development of non-communicable diseases [1] which has an impact on a social, economic, and health level. Mg^{2+} intake and bioavailability within a healthy population are subject to multiple factors that can affect overall Mg^{2+} status. These factors include Physicochemical and Dietary factors and may be considered when planning a healthy diet and determining DRIs for the population. Despite the research presented here, the European Food Safety Authority (EFSA) scientific panel found that data on Mg^{2+} interactions with other minerals, protein, and fiber are limited and unreliable for setting Dietary Reference Values (DRVs) for Mg2+ [7-13].

It is recommend lowering sodium intake and increasing consumption of fruits and vegetables, which are rich in minerals and alkalinizing properties. EAT-Lancet reference diet [46] which is rich in fruits and vegetables, with protein and fats sourced from plants and unsaturated oils from fish, and carbohydrates from whole grains [47], may be an option to achieve better intake and/or bioavailability of minerals. Adherence to this type of diet.

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