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Probiotic-driven advancement: Exploring the intricacies of mineral absorption in the human body

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ABSTRACT

The interplay between probiotics and mineral absorption is a topic of growing interest due to its great potential for human well-being. Minerals are vital in various physiological processes, and deficiencies can lead to significant health problems. Probiotics, beneficial microorganisms residing in the gut, have recently gained attention for their ability to modulate mineral absorption and mitigate deficiencies. The aim of the present review is to investigate the intricate connection between probiotics and the absorption of key minerals such as calcium, selenium, zinc, magnesium, and potassium. However, variability in probiotic strains, and dosages, alongside the unique composition of individuals in gut microbiota, pose challenges in establishing universal guidelines. An improved understanding of these mechanisms will enable the development of targeted probiotic interventions to optimize mineral absorption and promote human health.

Introduction

The term "probiotic" is an association between the Greek word "pro," which means "promoting", and "biotic," which means "life" (Ballini et al., 2019; Manzoor et al., 2022). According to the Food and Agriculture Organization (FAO), probiotics are viable microorganisms that thrive naturally in the gut and, when administered in adequate amounts, offer beneficial effects on human health. The mechanism of action of probiotics is multi-dimensional. They can colonize the gastrointestinal tract (GIT), host tissues, and the skin and beneficially alter the microbiota, helping to maintain intestinal bacteria balance (Katarzyna & Joanna, 2017; Manzoor et al., 2022). Probiotics are also implicated in the gut-brain axis, sustaining mental health and enhancing immune function (Markowiak-Kopeć & Śliżewska, 2020; Mohajeri et al., 2018).

The most known microorganisms for probiotic properties are the *Lactobacillus* family (*lactis*, *acidophilus*, etc.) *Bifidobacterium* (*bifidum*, *infantis*, etc.) *Streptococcus* group (*thermophilus*, *lactis*, etc.) and some yeasts, such as *Saccharomyces boulardii* (Manzoor et al., 2022; Nemes et al., 2022). They are commonly found in certain foods and dietary supplements as well. Recently, probiotics have received particular attention due to their ability to modulate nutrient absorption and act as a barrier against pathogenic bacteria in the intestinal mucosa, influencing the gut-brain axis (Bielik & Kolisek, 2021).

Probiotics may also be involved in the mineral metabolism (calcium (Ca), iron (Fe), magnesium (Mg), selenium (Se), potassium (K), copper (Cu), zinc (Zn), etc.), facilitating their absorption (Czajeczny et al., 2021). Research indicates that the level of minerals in the human body is primarily associated with its intake from the diet. At the same time, the functioning of the human body is related not only to the quantity of minerals but also to their proportion and the percentage of their absorption (Weyh et al., 2022). It was shown that probiotics can influence mineral absorption in the body. Some strains of probiotics have been found to enhance the absorption of certain minerals, while others may inhibit or have no effect on mineral absorption (Behera et al., 2020; Katarzyna & Joanna, 2017; Scholz-Ahrens et al., 2007). However, the mechanisms through which probiotics interact with mineral absorption are not yet fully understood and may vary depending on the specific strain of probiotics and the type of mineral.

It is important to note that the effects of probiotics on mineral absorption can vary depending on many factors, including the specific probiotic strain, the dose and duration of probiotic supplementation, the presence of other nutrients or dietary components, and individual

Abbreviations: Ca, Calcium; FAO, Food and Agriculture Organization; GM, Gut microbiota; SCFAs, Short-chain fatty acids; Se, selenium; Zn, zinc; K, potassium; WHO, World Health Organization.

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differences in the gut microbiota and overall health (Bielik & Kolisek, 2021). Therefore, more research is needed to understand the complex interactions between probiotics and mineral absorption and determine the optimal conditions to maximize potential benefits.

The aim of this paper is to provide a general overview of the absorption mechanism of minerals mediated by bacterial strains to explore the possible interconnection of probiotics with mineral homeostasis in human health.

Methods of literature selection

In order to identify publications on mineral absorption driven by probiotics, a literature search was conducted on Science Direct, PubMed, and Web of Science databases using the combinations of the key terms: "mineral absorption and probiotics", "calcium absorption and probiotics", "selenium absorption and probiotics", "magnesium absorption and probiotics", "zinc absorption and probiotics", "potassium absorption and probiotics"; also each mineral and the following combinations: "absorption mechanism of + each mineral", "clinical implications of probiotics in mineral metabolism". The review collected, analyzed and qualitatively re-synthesized information regarding (i) the importance of each mineral in the human body, (ii) the absorption mechanism, (iii) factors influencing the absorption mechanism, (iv) the link between probiotics and mineral absorption, and (v) clinical implications and future directions. The provided data encompasses publications from 2017 to 2023, consisting of a total of 100 research articles that are relevant and compatible with our topic of interest.

The intricate significance of minerals in the human body

The vital significance of Ca, Se, Zn, Mg, and K in the human body is highlighted by numerous researchers (Clase et al., 2020; Huang et al., 2022; Kanwar & Sharma, 2022; Kieliszek & Bano, 2022; Kodama et al., 2020; Minich, 2022; Raveschot et al., 2020; Rizzoli & Biver, 2020; Trapani et al., 2022; Zoroddu et al., 2019). These minerals are essential for our daily nourishment (Weyh et al., 2022). They are chemical elements that play a structural role in the human body and are indispensable for several metabolic functions (Katarzyna & Joanna, 2017).

Minerals are recognized as structural materials for bones, which regulate hydric balance and influence muscle and nerve function (Weyh et al., 2022). They are chemical elements that play a structural role in the human body and are indispensable for several metabolic functions (Katarzyna & Joanna, 2017). Hormones, enzymes, and other bioactive components depend on the catalytic action of minerals. Similarly, minerals are connected to the proper functioning of the immune system, influencing susceptibility to infections and even the development of chronic diseases (Bielik & Kolisek, 2021; Weyh et al., 2022) such as neurodegenerative diseases (Mitrea et al., 2022), osteoporosis (Gholami et al., 2022; Tyagi et al., 2018), diabetes (Steinbrenner et al., 2022), etc.

Most individuals can provide the body with sufficient amounts of vital minerals through a balanced diet. However, an increasing number of people are at risk of mineral deficiencies due to particular life circumstances (e. g., patients with chronic diseases, women during pregnancy, the elderly, vegetarians, vegans, etc.) or various lifestyle habits (e. g., poor sleeping habits, unhealthy dietary choices, etc.). Around 50 % of the worldwide population is affected by micronutrient malnutrition (Weyh et al., 2022). In addition, the World Health Organization (WHO) estimates that 2 billion people have micronutrient deficiencies (www.who.int).

The localization, or the specific location where absorption occurs for the abovementioned minerals, is illustrated in Fig. 1, providing visual clarity of each part of the intestine. Fig. 2 presents the mechanism of mineral absorption in the intestine. Mineral absorption in the gut occurs through paracellular and/or transcellular pathways. Specific transporters and pumps facilitate mineral uptake, such as TRPV6 for Ca (Khattar et al., 2022). Some minerals may undergo exchange with other ions during absorption. For example, Zn absorption can be influenced by the exchange with other divalent cations, such as copper, through transporters like ZIP4, responsible for Zn uptake in the intestine (Nishito & Kambe, 2018). Enterocytes synthesize proteins like calbindin D for Ca or TRPV6 (Khattar et al., 2022) and claudin for Mg (Luongo et al., 2018), aiding in mineral absorption. Absorbed minerals are transported across the basolateral membrane into the blood for systemic distribution via various mechanisms, including ATPase pumps and binding to carrier proteins like transferrin (Bielik & Kolisek, 2021).

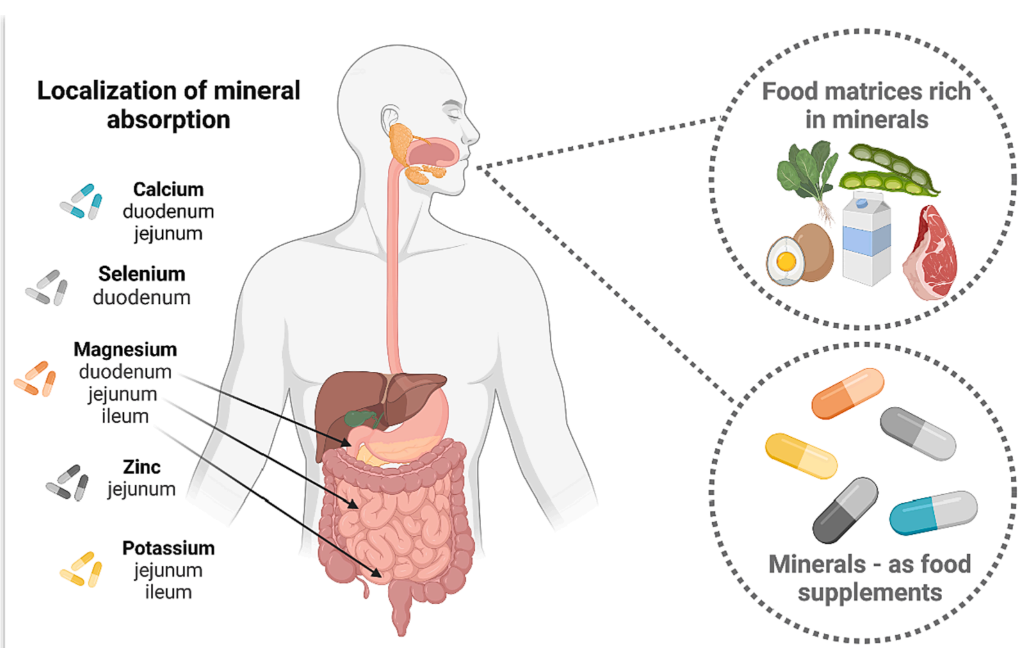

Fig. 1. Localization of mineral absorption despite the origin.

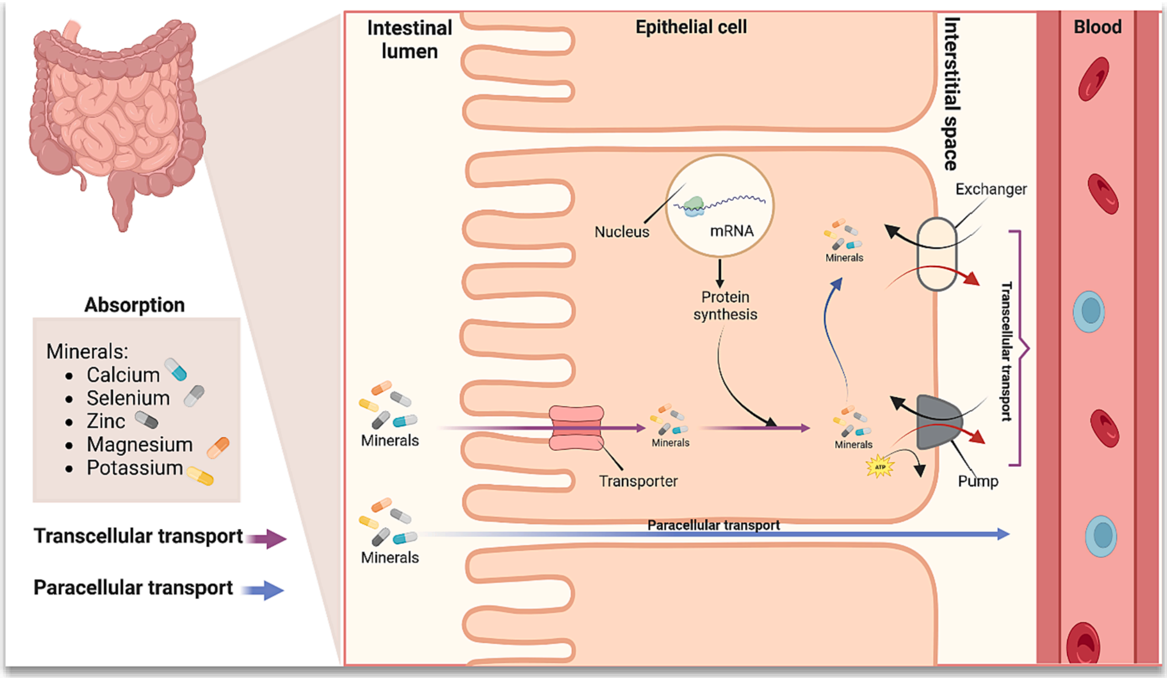

Fig. 2. The journey of mineral absorption in the human gut.

The dynamic interplay of the gut microbiota in mineral absorption

The GM, which refers to trillions of microorganisms that reside in the GIT (Sehrawat et al., 2021), can interact with minerals in several ways (Bielik & Kolisek, 2021). These microorganisms can enhance or inhibit the absorption of minerals in the digestive tract. The mechanisms by which GM can influence mineral absorption are complex and involve various interactions between microorganisms, minerals, and host cells (Bielik & Kolisek, 2021; Katarzyna & Joanna, 2017; Krausova et al., 2021; Peredo-Lovillo et al., 2020).

One way in which GM can interact with minerals is by producing enzymes that can break down complex minerals, making them more accessible to the host for absorption (D. Zhou et al., 2021). For example, bacteria in the gut produce phytases that humans or monogastric animals cannot endogenously produce. Phytases can break down phytic acid, a compound found in many plant-based foods that can bind to minerals and prevent their absorption (Nath et al., 2018). By breaking down phytic acid, these bacteria can release minerals like Ca, Mg, and Zn, making them available for absorption in the small intestine. Phytase hydrolyses phosphomonoester linkages in phytate during enzymatic conversion, resulting in an inorganic phosphate and a derivative of myo inositol phosphates (Scholz-Ahrens et al., 2007). The most known microorganisms as producers of phytase are *Bacillus subtilis, Bacillus coagulans* and different strains of the *Lactobacillus family (acidophilus, fermentum, plantarum, casei, brevis, etc.)*(Priyodip et al., 2017). Also, gut dysbiosis, an imbalance in the GM, can lead to impaired mineral absorption. The lack of beneficial bacteria in the gut can lead to decreased phytase production, resulting in decreased mineral absorption (Nath et al., 2018). It was observed that the phytases resulting from microorganisms are more effective in mineral absorption in animals than in plants or animal tissues (Nath et al., 2018; D. Zhou et al., 2021).

Another way in which GM can influence mineral absorption is by altering the gut environment (Markowiak-Kopeć & Śliżewska, 2020). The GM can produce short-chain fatty acids (SCFAs) as by-products of their metabolism of dietary fiber. Fermentation of dietary fibers increases the surface area accessible for mineral absorption (epithelial cell hypertrophy) in rats (Fardet, 2010). These SCFAs can lower the pH of the gut, which can increase the solubility of certain minerals (Mg, Ca, Se, Zn, etc.), making them more accessible for the host to absorb (Barkhidarian et al., 2021; Whisner et al., 2016). For example, reducing pH in the intestine leads to the dissolution of Ca ions, facilitating their delivery to cells through the paracellular pathway and regulating the mineral density of bones (Li et al., 2021). On the other hand, a high pH in the gut can reduce mineral absorption. Some medications, such as proton pump inhibitors (PPIs), can decrease Mg absorption by reducing stomach acid production, which is necessary to activate the Mg transporter TRPM6 (De Baaij et al., 2023; Leenders & Vervloet, 2019). GM can also produce other compounds that can bind to minerals and prevent their absorption, such as oxalates. Oxalate or oxalic acid can form salts with K ions and bind to Mg and Ca, restricting their absorption. Usually, these salts are insoluble at a neutral or high (alkaline) pH, but they freely dissolve in an acidic environment (Israr et al., 2013; Noonan, 1999).

Moreover, GM can affect the expression of genes involved in mineral absorption in the host cells. For instance, certain bacteria can promote the expression of genes that increase the host cell's ability to absorb iron (Fe). Inulin supplementation in pigs expanded the caecal microbial population in the genera *Bifidobacteria* and *Lactobacillus,* which further led to an upregulation of the expression of genes for Fe transporters, ferritin, and enzymes in the gut enterocytes (Tako et al., 2008).

GM can interact with minerals in the digestive tract through various mechanisms, including the production of enzymes that break down complex minerals, alter the gut environment, and affect gene expression in host cells. The complex interactions between gut microbiota and minerals affect nutrient status and overall health.

Highlights of the synergy between probiotics and mineral absorption

The potency of probiotics for optimal calcium absorption

It was shown that a healthy GM could increase Ca^{2+} absorption and modulate gut production of serotonin. The monoamine neurotransmitter, serotonin, is believed to regulate bone metabolism through its interaction with bone cells, possibly mediating the microbiota and bones (D'Amelio and Sassi, 2018). Other studies present conclusive evidence that probiotics improve bone health by modulating osteoblast bone formation by osteoblasts and osteoclast bone resorption (Ibrahim et al., 2022; Li et al., 2021; Xie et al., 2020).

One possible mechanism for higher absorption of Ca^{2+} in the intestine is increasing its bioaccessibility by administering probiotics (Bielik & Kolisek, 2021; Raveschot et al., 2020). In their study, Raveschot et al. reported that five *Lactobacillus* strains (10^9 CFU/mL) improved total Ca^{2+} transport after 24 h of contact with a differentiated Caco-2 cell monolayer. The *L. plantarum* strain increased cellular Ca^{2+} uptake in Caco-2 cells by 10 % compared to the control. *L. plantarum* modulated the transcellular pathway and enhanced the expression of vitamin D receptors and Ca transporters. While the *L. delbrueckii* strain performed on the paracellular path by modulating the expression of claudin-2 (Raveschot et al., 2020). Broilers predisposed to tibial dyschondroplasia were supplemented with *L. rhamnosus* strain. An improvement in the average growth and development of the tibial growth plate was observed alongside a restored Ca balance, suggesting that *L. rhamnosus* may represent a therapeutic procedure to treat leg disease in broilers (Liu et al., 2021). In a randomized double-blinded placebo-controlled study, symbiotic tablets were administered to healthy pediatric individuals (*Lactobacillus acidophilus, Lactobacillus plantarum, Bifidobacterium infantis, Bifidobacterium Lactis* – 45 × 10^9 CFU, and fructooligosaccharides) for ten weeks. An increase of 4 % in serum Ca level was observed for the symbiotic group, while, in the placebo group, there was a 7 % decrease in serum Ca level (Ballini et al., 2019).

Furthermore, in a six-month double-blind, randomized clinical trial, 78 postmenopausal women susceptible to osteoporosis were assigned to daily consume enriched yoghurt (Ca, Mg, Zn, vitamins, L-leucine, and *L. plantarum* 10^{10} CFU/mL) or control yoghurt. After six months, the group that ingested enriched yoghurt showed a significantly increased bone mineral density compared to the control group. The *L. plantarum* strain favoured the metabolism of Ca and the other micronutrients metabolism regarding bone mineral density and biochemical parameters (Morato-Martínez et al., 2020).

Another possible mechanism may be the production of several metabolites resulting from the probiotic fermentation of undigested carbohydrates (Li et al., 2021; Peredo-Lovillo et al., 2020). Short-chain fatty acids (SCFAs – e.g. propionate, butyrate, etc.) are the most studied metabolites and exhibit anti-inflammatory properties in the intestinal lining (Behera et al., 2020). The production of SCFAs can influence Ca absorption due to their ability to increase the surface area of the cecal villi and, thus, the absorption. SCFAs can enhance Ca metabolism by increasing the Ca-binding protein expression and paracellular transport. Likewise, a high level of SCFAs can lower the pH of the colon and cecum, improving Ca solubility (Barkhidarian et al., 2021). The reduction in pH leads to the dissolution of minerals and a facile delivery of Ca ions to cells through the paracellular pathway, regulating the mineral density of bones (Li et al., 2021). In a randomized dose–response trial on female adolescents, Ca absorption increased significantly after repeated consumption of soluble corn fiber. The SCFAs resulting after the fermentation of soluble corn fiber have decreased the pH and reduced calcium phosphate formation, enhancing Ca absorption in the intestine (Whisner et al., 2016). Also, SCFAs generated the hormone-insulin-like growth factor 1 (IGF-1, or somatomedin C), which benefits bone development, highlighting a link between the microbiota and bone metabolism (Yan & Charles, 2017). The *in vivo* capacity of SCFAs to regulate osteoclast metabolism and bone mass was tested in experimental mouse models. Propionate and butyrate were used in the experimental design as a treatment in mice and proved to increase bone mass and prevent inflammation-induced bone loss (Lucas et al., 2018).

All these studies support the feasibility and benefits of probiotic supplementation over standard therapy with Ca and vitamin D to improve bone health and overall Ca absorption mechanism.

Probiotics – A better path to enhanced selenium absorption

GM has been shown to influence Se status and SeP expression in mice. It was found that GM can isolate Se and limit its accessibility in the host. When Se amounts in the host are limitative, microorganisms can compete with the host for Se (Zhu et al., 2019). The *Lactobacillus plantarum* strain was enriched with Se and Zn, resulting in an increased blood Se level and a higher antioxidant activity (Kang et al., 2020).

Two microbial strains (*Enterococcus faecium* and *Streptococcus thermophilus*) were enriched with Se and administered to rats in conjunction with two other formulations without probiotics. Following the administration of Se-enriched strains, an increase in Se concentration was observed, with SeCys as the predominant form of Se, in the liver and kidneys of rats. Both tested strains proved to have great potential to improve the absorption mechanism of Se (Krausova et al., 2021). An increased absorption and distribution of Se into the pancreas was observed after administering Se-*B. longum* to rats, in comparison to the Na_2SeO_3 formulation (Zhao et al., 2020). Another study suggests that *B. longum* can biotransform inorganic Se into more bioactive forms of SePs and seven amino acids, making them more accessible to the human body (Zhu et al., 2019). Although Na_2SeO_3 exhibited the fastest time to reach the maximum absorbable concentration, supplementation with the organic Se formulations (selenized yeast and Se-*B. longum*) showed more efficient absorption, as these formulations had a higher accumulation and longer retention time of Se in the blood (Y. Zhou et al., 2020). Also, the co-administration of probiotics (*Lactobacillus acidophilus*, *Bifidobacterium bifidum* and *Bifidobacterium longum,* 2 × 10^9 UFC/day each) and Se (200 μg/day, sodium selenite) improved Se absorption of Se in the plasma for patients with Alzheimer's disease, resulting in better cognitive function (Barchielli et al., 2022).

These Se-enriched probiotics incorporated into foods can not only promote digestion and absorption, and enhance immunity needed by the human organism, but can also provide abundant organic Se source (mainly as SeP), which can meet human body needs from two perspectives of nutrient element supplementation and health care. Currently, Se-enriched microorganisms are mainly used in the nourishment of the livestock industry, with the ultimate purpose of improving the quality of meat products and providing organic Se that is conducive to human intestinal absorption (Yang & Yang, 2023).

Zinc Fortified: Probiotics power on improved zinc absorption

Recent studies suggest that certain probiotics may enhance Zn absorption in the body through different mechanisms. Some studies have found that Zn absorption from the diet may be increased through the expression of specific proteins involved in Zn transport across the intestinal wall. Other studies suggest that Zn absorption can be mediated through the production of SCFA, by lowering the gut's pH, which can increase the solubility and promote its absorption (Malyar et al., 2020; Mohammad Malyar et al., 2019).

An early research explicitly dealing with the *in vitro* absorption of Se and Zn internalized by probiotics and then tested on an intestinal cell culture model dates from 2012. Mogna et al., 2012 used a Caco-2 cell line that resembles human colonic cells as much as possible, equipped with specific enzymatic and transport systems for Se and Zn. They evaluated the vehicles of different forms of Se and Zn (Se/Zn + probiotics, organic and inorganic forms of these minerals) in a Transwell system. Experimental data indicate a significantly higher bioaccessibility of Se and Zn internalized by *L. buchneri* and *B. lactis* compared to the inorganic and organic forms tested. The results show the highest absorption and cell diffusion in Caco-2 for the formulations developed with probiotics (with Se/Zn). Se internalized by *L. buchneri* was 65 times more readily absorbed than seleno-l-cysteine, and Zn internalized by *B. lactis* was 31 times more readily absorbed than zinc sulphate. Also, improved *in vivo* bioaccessibility and systematic relevance were suggested (Mogna et al., 2012).

Recently, other researchers have focused on Zn-enriched probiotics, too (Jagan et al., 2018; Maares et al., 2022; Meng et al., 2022). In the study by Maares et al., experiments using a human *in vitro* digestion model and the Caco-2 *in vitro* intestinal cell model revealed that the intestinal Zn bioaccessibility of digested yeast biomass was comparable to the other Zn supplements, except for ZnO, which was slightly less bioaccessible. The Zn assimilation of *Saccharomyces pastorianus* was 5.9 mg Zn/g yeast, representing 0.6 % of the yeast biomass. Zn released from metabolized ZnYeast proved to be more accessible for biological processes within enterocytes, resulting in up-regulation of metallothionein, an intestinal biomarker of Zn status that significantly increased the cellular labile Zn pool (Maares et al., 2022).

The level of Zn in the blood can be influenced by the intake of dietary supplementation and is related to metabolism. The blood Zn level in the group of mice supplemented with Se/Zn internalized by *Lactobacillus plantarum* (SZ + Lp) was significantly higher than in the control group. The Zn concentration in blood was approximately 40 mg/L in the SZ + Lp group, while in the control group was a little over 20 mg/L (Kang et al., 2020). On the other hand, the enrichment of *L. plantarum* with Zn also proved to benefit the strain, by improving its physiological and functional characteristics. The Zn-enriched *L. plantarum* showed an increased acid production capacity and greater tolerance ability to bile salt, acid and H_2O_2. The antioxidant properties of the Zn-enriched strain improved significantly, along with the antioxidative enzyme activities. The *L. plantarum* strain proved to be a great carrier of Zn with possible application in the food industries (Meng et al., 2022).

Furthermore, another bacterial strain, *L. fermentum*, was studied in relation to Zn absorption. Interestingly, *L. fermentum* was shown to have the ability to biotransform the internalized inorganic Zn into its organic form, facilitating its absorption when administered to Wistar rats. An increased level of Zn was observed in serum, liver, femur bone and hair after 4 weeks of the administration of Zn-enriched *L. fermentum* (Jagan et al., 2018).

Thus, studies have shown that certain probiotics can enhance the absorption of Zn in the body through different mechanisms. Probiotics can increase the bioaccessibility and bioavailability of Zn, which can be attributed to the expression of specific proteins involved in Zn transport across the intestinal wall or the production of SCFA that lowers the gut's pH and promotes Zn solubility. The bioaccessibility of Zn can also be improved by biotransforming inorganic Zn into its organic form by certain probiotic strains. These findings suggest that Zn-enriched probiotics have the potential to be used as functional foods in the food industry and may provide a promising strategy to improve Zn nutrition and prevent Zn deficiency and related diseases.

Probiotics paving the way to optimal magnesium absorption

The relationship of Mg with probiotics has yet to be studied. Thus, the exact mechanisms by which probiotics enhance Mg absorption are not fully understood, but several ways and processes may be involved (García-Legorreta et al., 2020). The strain HN001 of *L. rhamnosus* was shown to improve Ca and Mg absorption in growing rats by improving bone density at spine and femur levels after 12 weeks of daily intake, compared to the control group (Kruger et al., 2009). Possible action mechanisms may be linked to the bacterial production of SCFAs by lowering the pH in the intestine, which may further increase the mineral solubility. Increased enterocyte proliferation expands the area of absorption in the rat's large intestine and facilitates Ca and Mg absorption. SCFAs may also promote the growth of beneficial bacteria in the gut, which can further facilitate Mg absorption (Kruger et al., 2009; Louzada et al., 2019).

Another potential mechanism is the improvement of intestinal motility by probiotics (Dimidi et al., 2017). This can increase the time Mg is in contact with the gut lining, allowing a more efficient absorption (Duttaroy, 2021; Noland et al., 2020). Additionally, probiotics can help reduce inflammation in the gut, improving overall intestinal health, and increase nutrient absorption (Cristofori et al., 2021). The transcellular pathway involves the active transport of Mg ions through the intestinal lining through specialized transport proteins. Some studies have suggested that probiotics can enhance the expression and activity of these transport proteins, leading to increased Mg absorption. On the other hand, the paracellular pathway involves the passive diffusion of Mg ions through the tight junctions between gut epithelial cells. Probiotics may help to regulate the tightness of these junctions, which can impact the movement of Mg ions and other nutrients across the gut lining (Kruger et al., 2009).

A few studies have investigated the relationship between probiotics and Mg absorption. For example, in a pilot study with 12 patients diagnosed with SSRI-resistant depression, a mixture of probiotics (10 billion CFU *L. acidophilus*/4 billion CFU *B. bifidum*/6 billion CFU *S. thermophiles)* and magnesium orotate (1600 mg) were tested. The intervention with the mix was two daily doses for 8 weeks. After 8 weeks, it was followed up at 16 weeks. The combination of probiotics and magnesium orotate was chosen due to the involvement of Mg in the proper functioning of the brain and the ability of probiotics to modulate the gut-brain axis. The reported results show a mean Beck Depression Inventory (BDI) score of 16.1, which means mild depression. Also, the energy levels and the well-being of the patients were improved. The administration of the mixture proved to have a significant anti-depressive effect with the help of probiotics which enhanced Mg absorption (Bambling et al., 2017).

Moreover, functional foods like prebiotics (mannan oligosaccharide), probiotics (*L. acidophilus, Enterococcus faecium, B. thermophilum,* and *B. longum* (2–5 10^9 UFC each)) and symbiotics (prebiotic + probiotic) proved to improve several health parameters (Mg, P, Ca status in bone composition, bone mineral density (BMD), bone mineral content (BMC), resilience, stiffness) when administered to rats exposed or not exposed to passive cigarette smoke. The concentration of Mg increased considerably in the femur of rats that received the formulation containing only probiotics, whether they were exposed to cigarette smoke, reaching the highest value (6.73 mg/g) compared to the other groups and the other formulations assigned. This group enhanced all the health parameters (Louzada et al., 2019). Another 30-day experiment reveals infant formulas supplemented with *B. bifidum* and *B. longum* can increase Mg bioavailability in rats. It was shown that Mg apparent absorption and retention ratios were higher than 80 % throughout the first balance period of the experiment (Dario et al., 2013).

On the other hand, a dietary Mg deficiency was correlated with reduced microbial diversity and a substantially modified microbiota after six weeks of experiment with mice (C57BL/6 mice) using the light/dark box anxiety test. After six weeks, the mice showed anxiety-like behaviour, which was determined by the low latency to move in the lightbox. A homoeostatic GM-brain axis may be disrupted by a Mg deficit (Pyndt Jørgensen et al., 2015). Additionally, dietary Mg supplementation in the case of no mineral deficiency may also lead to intestinal dysbiosis development (García-Legorreta et al., 2020).

Specific strains of probiotics may play a role in the absorption of Mg, along with individual differences in the composition of GM and overall gut health. The dose and duration of probiotic supplementation may also impact their effectiveness in increasing Mg absorption. However, more research is needed to fully understand the mechanisms underlying the relationship between probiotics and Mg absorption and determine the most effective strains and doses for this purpose.

Improved potassium absorption empowered by probiotics

Probiotics may be involved in K absorption through various mechanisms, including modulating GM's composition and improving gut health. For instance, probiotics may help to regulate the tightness of tight junctions between gut epithelial cells, thereby facilitating the paracellular transport of K ions.

Factors that may influence K absorption driven by probiotics can be related to the specific strains and doses of probiotics used, also individual differences in GM composition may interfere with the absorption mechanism. Other factors that may alter K absorption include the presence of other nutrients, such as sodium, that can compete for absorption.

Several studies have investigated the relationship between probiotics and K absorption (Cao et al., 2020; El-Sayed & Mousa, 2019; Sadeek, 2018). For example, *Bacillus subtilis* was tested in growing Barki lambs to investigate its potential effect on body growth and mineral concentrations. After 30 days of experiment, the serum K concentration in the group fed a basal diet supplemented with probiotics increased to 4.9 mmol/L, while in the control group it was 3.9 mmol/L. Also, animal growth performance was improved, in terms of body weight, height and length, chest girth, and anamorphosis indices (El-Sayed & Mousa, 2019). The impact of probiotic supplementation was also evaluated in a double-blind, randomised, placebo-controlled study in patients with chronic kidney disease. After 3 months of probiotic administration (*Streptococcus thermophilus*, *Lactobacillus acidophilus* and *Bifidobacteria longum),* an increase in K concentration was observed from 4.4 mmol/L to 4.8 mmol/L. The results suggest that the probiotic intervention did not have a notable influence on the absorption of K in this particular study (Borges et al., 2018). *L. casei* Shirota was tested on rats subjected to oxidative stress and with chronic renal failure. After 8 weeks of treatment only with the probiotic strain, an increased concentration of serum K was observed. A possible mechanism of the enhanced absorption of K may be the ability of *L. casei* Shirota to modulate gut microbiota. *L. casei* can promote the growth and activity of specific bacteria that play a role in the absorption of K or that it directly affected the absorption process (Sadeek, 2018).

Moreover, another study explored the effects of probiotics on intestinal digestion and absorption, antioxidant capacity, and microbiota composition in fattening pigs. The administration of *Bacillus amyloliquefaciens* to these pigs resulted in favourable changes in the activity of digestive enzymes within the intestinal tract. A positive impact on Na^+/K^+-ATPase enzyme activity was observed. This enzyme plays a crucial role in maintaining electrochemical balance in cells, being responsible for pumping sodium ions (Na^+) out of the cell and K ions (K^+) into the cell. Thus, the Na^+/K^+-ATPase enzyme contributes significantly to maintaining normal functionality of intestinal cells and facilitating nutrient absorption (Cao et al., 2020).

A multi-strain probiotic mix (*L. delbrueckii* ssp. *bulgaricus, L. acidophilus, L. helveticus, L. delbrueckii* ssp. *lactis, Streptococcus thermophilus* and *Enterococcus faecium*) was tested on the internal milieu of broiler chickens after oral administration. Regarding K absorption, the study found that probiotic supplementation had a remarkable effect on enhancing K absorption in broiler chickens. K level in serum was 5.37 mmol/L in the supplemented group, compared to the control group, where K level was 4.91 mmol/L. The oral intake of this combination of probiotic strains had an important impact on improving K absorption within the broiler chickens' GIT (Capcarova et al., 2011).

Interestingly, the addition of *L. rhamnosus* in white soft cheese increased the mineral concentration. The K concentration is the white cheese containing *L. rhamnosus* was 7.98 mg/L, while in the control was only 6.33 mg/L. This growth can be attributed to the intensified enzymatic conversion, predominantly proteolysis and lipolysis (Dafalla et al., 2021). The effect of *L. rhamnosus* supplementation was considered for an *in-vitro* experiment regarding the availability of minerals, including K, from cheeses and cheese-like products. The results suggested that the presence of the probiotic strain, *L. rhamnosus*, increased K availability by 36 % in cheese-like products that ripened for six weeks, while in Swiss-type cheese only 11 %. Probiotic supplementation seemed to enhance the bioavailability of K in these products, meaning an increased bioaccessibility of K for absorption *in vivo*. Further research is needed to determine the exact mechanisms by which *L. rhamnosus* alters K absorption and to validate these results in human studies (Aljewicz & Cichosz, 2015).

Overall, while the evidence for the involvement of probiotics in K absorption and utilization is promising, more research is needed to fully understand the mechanisms and optimize the use of probiotics for this purpose. It is also important to note that individual differences in GM composition and overall gut health may impact the effectiveness of probiotics for enhancing mineral absorption, including K.

Table 1 presents a concise overview of research findings linking minerals, probiotics, study methodologies, and their respective impacts on health.

Factors influencing probiotic effects on mineral absorption

The effectiveness of probiotics in enhancing mineral absorption can be influenced by several factors. These factors include the specific strain of probiotic used, dosage, timing of administration, strain-mineral affinity, and individual differences among people (Barkhidarian et al., 2021; Bielik & Kolisek, 2021; Rizzoli & Biver, 2020).

Different strains of probiotics may have varying effects on mineral absorption. Each strain has unique characteristics and may interact with minerals in different ways (Chen et al., 2022; Ferreira et al., 2021; Mm et al., 2022). Some strains may produce enzymes that enhance the bioavailability of minerals, while others may not have the same effect. These enzymes are involved in breaking down complex minerals into more absorbable forms. For instance, lactic acid bacteria produce phytase, an enzyme, which aids in the release of minerals from plant-based products, making them bioaccessible for absorption (D. Zhou et al., 2021). Also, it was shown that some strains may have specific interactions with certain minerals. For example, it was found that Mg absorption may be influenced by *L. plantarum, L. reuteri, L. rhamnosus, L. paracasei*, and *L. acidophilus,* while Se absorption may be mediated by *S. thermophilus, Enterococcus faecium, B. longum* and *L. plantarum* and some yeasts, etc (Bielik & Kolisek, 2021; Krausova et al., 2021). These microorganisms (and others) may facilitate the solubility, transport, or uptake of minerals in the gut, leading to improved absorption (Dario et al., 2013). Furthermore, probiotic strains can modulate the gut environment (Duttaroy, 2021), including pH levels (Meng et al., 2022), production of metabolites (Lucas et al., 2018), and competition with other gut microbes (Ferreira et al., 2021). Different strains may create distinct gut environments, impacting mineral absorption to varying degrees. These changes can modify the solubility of minerals. Therefore, selecting the appropriate probiotic strain is critical to maximize the potential benefits of mineral absorption (Bielik & Kolisek, 2021; Duttaroy, 2021; Meng et al., 2022).

The dosage of probiotics can play a role in their efficacy. Higher doses of probiotics may lead to more significant effects on mineral absorption. However, the optimal dosage can vary depending on the specific strain and individual factors (Katarzyna & Joanna, 2017; Skrypnik et al., 2019). Probiotics have the ability to adhere to the intestinal membrane, competing with pathogenic bacteria for binding sites and nutrients, including minerals (Ballan et al., 2020; Niranjan et al., 2023). Higher dosages of probiotics are able to restrict pathogenic bacteria growth, thus indirectly enhancing mineral absorption (Ballan et al., 2020; Niranjan et al., 2023; Rabetafika et al., 2023). A low level of probiotics in the gut environment can modify mineral absorption by increasing the pH and lowering the production of certain metabolites, such as SCFAs (De Baaij et al., 2023; Leenders & Vervloet, 2019). These SCFAs facilitate the dissociation of minerals into more absorbable forms (Ashaolu, 2020; Ballan et al., 2020; Markowiak-Kopeć & Śliżewska, 2020). By creating a more favourable environment, probiotics may increase the chances of minerals being released and absorbed by the host (Bielik & Kolisek, 2021; Suliburska et al., 2021). Also, higher doses of probiotics can influence gut motility and transit time, potentially altering the time available for minerals to be absorbed (Dimidi et al., 2017). Rapid transit time may limit the contact time between minerals and the intestinal membrane, reducing the opportunity to be absorbed (Barkhidarian et al., 2021). It is important to note that the impact of the administered dose of probiotics on mineral absorption is not fully

Table 1
Amplified mineral bioaccessibility in the gut and exploring the involved mechanisms.

Mineral	Probiotic	Type of study	Nr. of subjects	Intervention	Mechanism	Outcome	Ref.
Calcium	Konjac Oligosaccharides improved microbial genera of *Lactobacillus, Bifidobacteria, Mucispirillum, Alistipes.*	*In vivo* (on mice)	60	8 weeks	• The administration of konjac oligosaccharides modulated the gut environment by facilitating the growth of *Lactobacillus, Bifidobacteria, Mucispirillum* etc.	• Improved skeletal mechanical strength • Modified GM, and gut metabolites • Increased bone mass • Enhanced Ca absorption.	(Ai et al., 2021)
	Symbiotic yoghurt (inulin (4 g) and *L. rhamnosus* (10^7 CFU/mL)	*In vivo* (Young adult women)	30	3 weeks	• The symbiotic combination may have contributed to better nutrient-nutrient interaction, improving Ca absorption, and showing potential implications for bone health in young adult women.	• Increased Ca bioavailability in the gut • supporting overall bone health • promoting optimal Ca utilization	(Cornes et al., 2022)
Selenium	*L. plantarum* 10^{12} CFU/day	*In vivo* (mouse model)	32	4 weeks (oral administration)	• Biotransformation of inorganic Se into bioactive organic Se	• Increased blood Se level in mice • Increased utilization of seleno-amino acids.	(Kang et al., 2020)
	Streptococcus thermophilus and *Enterococcus faecium* 10^9 CFU/g	*In vivo* (rat model)	48	58 days	• Both Se-enriched strains supplied the micronutrient in a more bio-accessible form and less toxic.	• Higher Se concentrations in the liver and kidneys of rats • Improved antioxidant status in animals	(Krausova et al., 2021)
	L. acidophilus and *S. cerevisiae* 10^9 CFU/mL	*In vivo* (Wistar rats)	60	30 days	• Bioaccumulation of Se and Zn by the probiotic strains	• Increased enzyme activity (glutathione-peroxidase and superoxide-dismutase). • The expression of genes (GPx1 and SOD1) was also increased.	(Malyar et al., 2020)
Zinc	*L. acidophilus* and *S. cerevisiae* 10^9 CFU/mL	*In vivo* (Wistar rats)	36	40 days	• Both Zn-enriched probiotic strains improved Zn absorption	• Enhanced growth performance in Wistar rats by improving: • antioxidant activity, • immune function, • liver, heart, and kidney gene expression • intestinal morphological characteristics.	(Mohammad Malyar et al., 2019)
	L. fermentum	*In vivo* (Wistar rat)	48	4 weeks	• The probiotic strain proved to have the ability of internalizing and biotransforming inorganic Zn into its organic form, facilitating the absorption.	• Increased level of Zn in serum, liver, femur bone and hair in Wistar rats.	(Jagan et al., 2018)
Magnesium	*L. rhamnosus*	*In vivo* (rat model)	62	12 weeks of daily intake	• Production of SCFAs which may lead to mineral solubility	• Improved bone density at spine and femur level	(Kruger et al., 2009)
	Lactobacillus acidophilus, Enterococcus faecium, Bifidobacterium thermophilum and *Bifidobacterium longum*	*In vivo* (rat model)	64	189 days	• By a reduction in the inflammatory response • increased levels of SCFAs • increased secretion of bacterial factors and intestinal hormones.	• Mineral content improved in animal model. • BMD, BMC, resilience, and the size of area of the femoral diaphysis were also improved in rats in the growth phase.	(Louzada et al., 2019)
Potassium	*Bacillus subtilis*	*In vivo* (on Barki lambs)	12	30 days	• Production of metabolic substrates and modulation of GM	• Increased serum K concentration in Barki lambs • improved animal growth performance	(El-Sayed & Mousa, 2019)
	Streptococcus thermophilus, L. acidophilus and Bifidobacterium longum	*In vivo* (on humans)	46	8 weeks	• Modulating GM and promoting beneficial bacterial growth	• Higher level of K in serum	(Borges et al., 2018)

understood and may vary depending on factors like the specific strain involved, individual GM composition, and the type of minerals involved. Additionally, the effect may differ between individuals, and what constitutes a “higher dosage” can vary based on various factors. However, homeostasis in the gut is desired to enhance mineral absorption (Bielik & Kolisek, 2021; Śliżewska et al., 2021).

The timing of probiotic administration can impact their interaction with minerals. For example, taking probiotics along with a meal enriched with minerals may enhance their absorption (Jagan et al., 2018; Mohammad Malyar et al., 2019). This is because the presence of food can provide an environment conducive to the survival and activity of probiotic bacteria, allowing them to exert their effects on mineral absorption. On the other hand, taking probiotics on an empty stomach or alongside the intake of antibiotics may not provide the same benefits (Cao et al., 2020). Moreover, the absorption and metabolism of minerals can follow circadian rhythms, the 24-hour biological cycles regulating various bodily functions (Noland et al., 2020). Some research suggests that mineral absorption may vary throughout the day. By considering the timing of probiotic administration in relation to these circadian rhythms, it is possible to optimize mineral absorption during periods when it is naturally more efficient (Turroni et al., 2020). Therefore, considering the timing of probiotic consumption in relation to meals can influence their efficacy.

Individual uniqueness, such as genetic factors, GM composition, and overall health status, can influence how probiotics interact with minerals and their efficiency (Ballan et al., 2020). Each human being has a tailored GM, which can respond differently to the supplementation with probiotics. The efficiency of probiotics can also be impacted by other factors, such as pre-existing disorders affecting the gut, pharmaceutical use, and food in general (Manzoor et al., 2022). Genetic variations may also influence a person's ability to digest and metabolize minerals. The most effective probiotic therapies can be created by considering these individual variances (Ballan et al., 2020; Mohajeri et al., 2018).

Recent studies highlight the potential influence of nanoscale metal oxides on gut health, potentially inducing Fenton-like effects and oxidative stress (Stuparu-Cretu et al., 2023). This stress may disrupt the balance of the gut microbiota (GM), posing questions about its wider impact on mineral absorption and probiotic efficacy (Bielik & Kolisek, 2021; Pambianchi et al., 2022; Stuparu-Cretu et al., 2023). Oxidative stress is a critical factor affecting mineral absorption in the intestines, modifying the environment, and potentially impacting bioaccessibility and uptake of essential minerals. The disrupted GM, caused by Fenton-like effects, introduces a novel perspective on the intricate factors influencing nutrient metabolism (Pambianchi et al., 2022). Furthermore, the connection to probiotics adds depth to this complex network. Probiotics may play a role in mitigating the consequences of oxidative stress. Exploring how nanoscale metal oxides influence oxidative stress, alter the GM, and subsequently impact mineral absorption offers a rich field for scientific investigation. Understanding how probiotics could alter these impacts presents opportunities for therapies aimed at maintaining optimal gut health (Bielik & Kolisek, 2021; Yu et al., 2021).

In summary, the efficacy of probiotics in improving mineral absorption can be influenced by strain variants, dosage, timing of administration, and individual uniqueness. Considering these factors when selecting and administering probiotics can optimize their potential benefits on mineral absorption. However, it is important to highlight that more research is needed to fully understand the complex interactions between mineral absorption and probiotics intake to provide specific recommendations (Barkhidarian et al., 2021; Bielik & Kolisek, 2021; Manzoor et al., 2022).

Clinical implications and future directions

The clinical implications of probiotics in mineral absorption refer to the possible practical applications and advantages of utilizing probiotics to improve or optimize the absorption of minerals in a clinical setting. Recently, probiotics gained attention for their ability to enhance the bioaccessibility and bioavailability of minerals (Jagan et al., 2018; Krausova et al., 2021; Manzoor et al., 2022). The abovementioned strains can produce enzymes, organic acids, or other metabolites that promote mineral availability and solubility in the GIT. By enhancing mineral bioaccessibility, probiotics can potentially improve their absorption and utilization by the body, leading to a better nutritional status (Bielik & Kolisek, 2021; Borges et al., 2018; Lucas et al., 2018).

Probiotics may represent a complementary approach to address mineral deficits in individuals with poor mineral intake or absorption. By increasing the absorption and usage of minerals, probiotics could aid in mitigating or preventing these deficiencies, which can have meaningful health implications (Krausova et al., 2021; Morato-Martínez et al., 2020). For instance, probiotics have been considered for their potential role in improving the absorption of several minerals, like Ca, Se, Zn, Mg, K, etc. Adequate mineral absorption, particularly Ca and Mg, is essential to maintain optimal bone health in order to prevent health conditions like osteoporosis (Rizzoli & Biver, 2020; Suliburska et al., 2021). It was shown that probiotics could contribute to improving bone mineral density and lower the risk of fractures. This may be relevant in clinical trials with populations at risk of bone-related disorders, like post-menopausal women or older adults (Locantore et al., 2020; Rizzoli, 2019). In clinical settings where mineral supplementation or nutrient therapy is prescribed, probiotics may play a supportive role. The co-administration of probiotics with mineral supplements or the intake of mineral-enhanced probiotics could improve the absorption and utilization of the supplemented minerals, potentially optimizing the effectiveness of nutrient therapy and improving health status (Chen et al., 2022).

Furthermore, gastrointestinal disorders that affect nutrient absorption, like celiac disease, irritable bowel syndrome, or inflammatory bowel disease, may benefit from probiotic administration to improve mineral absorption. Probiotics can modulate GM, reduce inflammation, and improve gut barrier function, which may positively impact mineral absorption in these health conditions (Chen et al., 2022; Jurášková et al., 2022; Manzoor et al., 2022). Different probiotic strains may have varying effects on mineral absorption, and individual GM composition may influence the interactions between probiotics and minerals. Understanding the specific needs and characteristics of each individual can aid in tailoring probiotic interventions for optimizing mineral absorption (Bielik & Kolisek, 2021; Czajeczny et al., 2021).

There is a need for standardized protocols and guidelines for probiotic use in mineral deficiency. Identifying specific probiotic strains with demonstrated efficacy for different minerals and clarifying the mechanisms by which probiotics influence mineral absorption, utilization, and homeostasis would be valuable. Understanding these mechanisms would be helpful in developing targeted interventions (Barkhidarian et al., 2021; Nowicki & Pories, 2023). Also, determining the optimal dosages and duration of interventions for probiotic administration in mineral deficiencies is essential. Further studies are needed to investigate the dose–response link and the long-term effects of probiotics regarding mineral status (Barkhidarian et al., 2021). Large-scale, well-controlled clinical trials are warranted to evaluate the efficacy of probiotics in preventing and treating mineral deficiencies in different populations. Investigating potential interactions between probiotics and dietary factors, medications, or individual variations in GM composition is fundamental for optimizing probiotic interventions for mineral deficiencies (Bielik & Kolisek, 2021; Davis et al., 2020). Addressing these gaps will contribute to a clearer understanding of how probiotics can be effectively utilized in the prevention and treatment of mineral deficiencies.

Conclusions

The present review study highlights the vital importance of minerals in the human body, focusing on Ca, Se, Zn, Mg, and K. A comprehensive examination investigates the complex involvement of GM in absorbing these essential minerals, revealing the critical role these microscopic organisms play. In addition, this research explores the potential impact of probiotics, offering promising approaches for improving mineral absorption. Dedicated sections focusing on probiotics and their link to individual minerals provide valuable insights into the potential benefits of incorporating these beneficial bacteria into our dietary habits. This study contributes to understanding the complex interaction between GM, probiotics, and mineral absorption, increasing the knowledge of how these interrelated factors can influence human health and nutrition. These insights hold great promise for developing strategies that could positively impact human health by addressing potential mineral deficiencies and promoting optimal nutritional outcomes. Ultimately, this review paper opens the way for future exploration and research in this exciting field, encouraging further investigation into the complex mechanisms underlying mineral absorption and the potential for harnessing the ability of probiotics to improve overall health and vitality.

Credit authorship contribution statement

Rodica-Anita Varvara: Conceptualization, Writing – original draft, Writing – review & editing. **Dan Cristian Vodnar:** Conceptualization, Supervision, Validation, Visualization, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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