Carbohydrate malabsorption and non-celiac gluten/wheat Sensitivity: The role of probiotic biomodulation

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***Abstract**: In recent years, cases of food hypersensitivity reactions in the Western population have significantly increased, with over 50% of patients with functional gastrointestinal disorders (FGID) believing that food triggers their symptoms. The main culprits include FODMAPs (Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols) and specific protein components of wheat, such as gluten and amylase/trypsin inhibitors (ATIs).*

Gastrointestinal symptoms related to carbohydrate malabsorption stem from two primary mechanisms. First, unabsorbed carbohydrates can feed certain gut bacteria, leading to fermentative dysbiosis and gas production, which causes bloating and abdominal distension. Second, a diet rich in unabsorbed sugars draws water into the intestinal lumen, accelerating transit and resulting in diarrhea.

Adverse reactions to gluten include celiac disease, wheat allergy, and non-celiac gluten/wheat sensitivity (NCGS/WS). The latter triggers both intestinal and extra-intestinal symptoms, which improve upon gluten withdrawal. Recent studies suggest that, in addition to gluten, other wheat components, such as ATIs and FODMAPs, can contribute to symptom exacerbation. NCGS/WS is associated with intestinal dysbiosis and immune alterations. Although a gluten-free diet is currently considered the only available therapeutic strategy, it may negatively impact gut microbiota and the bioavailability of minerals and vitamins.

Recent research suggests the use of strain-specific probiotics to improve fermentative dysbiosis, reducing gas-producing species and enhancing the digestion and absorption of carbohydrates, gluten proteins, and micronutrients. In conclusion, an integrated approach combining a low-FODMAP diet (LFD) with specific probiotics could be an effective strate-

gy for managing carbohydrate malabsorption symptoms in FGID, restoring intestinal homeostasis, and counteracting associated microbial hyperfermentation.

***Key words**: Carbohydrate Malabsorption, low FODMAP diet, Non-Celiac Gluten/Wheat Sensitivity, Micronutrient malabsorption, Microbiota, Probiotics.*

Microbiota and carbohydrate malabsorption

It is now well known that in a typical Western diet, carbohydrates represent a vital source of energy but, in certain individuals, can pose ongoing challenges in terms of digestion and absorption. Among various dietary factors, the quality of carbohydrates – considering their nature, sugar content, and dietary fiber – has been widely regarded as a potential modulator of the risk of non-communicable chronic diseases (NCDs). Recent systematic reviews of randomized clinical trials (RCTs) and prospective observational studies conducted on adults have found that higher consumption of whole grains, vegetables, and fruits is associated with a reduced risk of NCDs and related mortality.

The World Health Organization (WHO) recommends that carbohydrate intake should primarily come from whole grains, vegetables, fruits, and legumes, with an adult daily intake of at least 400 g/day of vegetables and fruits and 25–35 g/day of dietary fiber. For children, the recommendation includes fruit and vegetable intake ranging from 250 to 400 g/day and fiber intake between 15 and 25 g/day (*Carbohydrate Intake for Adults and Children*, s.d.).

Despite the necessity for regular and consistent intake of adequate amounts of carbohydrates in the diet, they are often reported by patients as potential causes of adverse food reactions. Over the past two decades, cases of adverse food reactions have risen significantly, with 40% to 84% of patients with functional gastrointestinal disorders (FGIDs), particularly those with irritable bowel syndrome (IBS), identifying foods as significant triggers for their symptoms. Carbohydrates are implicated as a source of symptoms in 70% of patients, and gluten-based products are identified as culprits by approximately one in four patients (Makharia *et al.*, 2018).

A recent literature review indicates that, for many patients, in addition to gluten, FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols) – particularly lactose – can contribute to bloating and/or abdominal distension associated with pain and alterations in intestinal transit as a consequence of maldigestion and malabsorption (Zingone *et al.*, 2023).

It is believed that the gastrointestinal symptoms of carbohydrate malabsorption are primarily caused by two factors. First, when carbohydrates are not properly

broken down and absorbed, they may act as fuel for gut bacteria, contributing to fermentative dysbiosis with excessive production of hydrogen, methane, and carbon dioxide, which are responsible for bloating and/or abdominal distension. Second, a diet rich in unabsorbed sugars attracts significant amounts of water, increasing the osmotic load, leading to accelerated transit of the food bolus and diarrhea.

These reactions significantly compromise patients' quality of life and necessitate long-term dietary restrictions. While these restrictions can improve clinical and symptomatic profiles, they expose patients to alterations in gut microbiota biodiversity and the malabsorption of micronutrients (Omer & Quigley E.M.M., 2018).

FODMAPs are short-chain carbohydrates that include lactose, fructose, polyols (sorbitol and mannitol), fructans, galacto-oligosaccharides, stachyose, raffinose and verbascose (RFO) naturally present in a wide range of foods, including fruits, vegetables, cereals, legumes, dairy products, and both natural and artificial sweeteners (Ispiryan *et al.*, 2022).

These molecules are poorly absorbed in the small intestine due to a slow transport mechanism or an ineffective or reduced enzymatic activity. Once ingested, they remain partially undigested in the intestinal lumen, particularly in the colon, where, after fermentation by the gut microbiota, they release gases and attract water through osmotic effects. This process, in predisposed individuals, leads to the onset of bloating and/or abdominal distension, visceral hypersensitivity, abdominal pain, and alterations in transit, particularly diarrhea.

A dietary restriction of FODMAPs can improve symptoms in a large number of patients with irritable bowel syndrome (IBS), and several controlled clinical trials have demonstrated the superiority of the Low-FODMAP Diet (LFD) compared to control diets in IBS patients. The most significant effects of the diet include improvements in bloating and abdominal pain, as well as normalization of bowel habits, with both diarrhea and constipation associated with IBS regressing (Algera *et al.*, 2022; Carbone *et al.*, 2022; Halmos *et al.*, 2014; Holtmann *et al.*, 2017).

Despite the numerous clinical and symptomatic benefits, the Low-FODMAP Diet is not without medium to long-term consequences. In recent years, several authors have investigated the nutritional adequacy of the LFD. Fiber deficiencies are the most common, caused by a reduction in the intake of plant-based foods. Furthermore, calcium intake has been found to be lower when dairy products are excessively excluded. Regarding vitamin intake, the risk of deficiencies is linked to a strict reduction in vegetable and fruit consumption in the diet (Carbone *et al.*, 2022; Sultan *et al.*, 2022; Whelan *et al.*, 2018).

Another highly significant aspect is that the LFD induces alterations in gut microbiota biodiversity, with a significant reduction in the Bifidobacterium genus,

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which is widely considered in the scientific literature as a marker of general eubiosis in the intestinal microbial ecosystem (Rinninella *et al.*, 2019; van Lanen *et al.*, 2021).

Lactose intolerance (LI) is among the most common disaccharidase deficiencies (lactase, sucrase, and maltase). It presents as a clinical syndrome characterized by specific signs and symptoms, including abdominal pain, bloating, and diarrhea triggered by the consumption of this sugar in individuals with lactose malabsorption (LM).

Normally, lactose, a disaccharide, is broken down into glucose and galactose by the enzyme lactase, located on the brush border of the small intestine. Lactase deficiency is common in healthy individuals, resulting in malabsorption when consuming milk or lactose-containing foods, and it can arise from various causes.

The most prevalent cause is "primary lactase deficiency" or "lactase non-persistence", characterized by a gradual decline in lactase enzyme activity with age (Bayless *et al.*, 2017). In addition to this form of hypolactasia, lactose intolerance may also result from "secondary lactase deficiency", caused by conditions such as gastroenteritis, chemotherapy, antibiotic use, celiac disease, inflammatory bowel disease, malnutrition, or conditions that reduce the absorptive surface, such as short bowel syndrome. Lactase deficiency, or hypolactasia, leads to lactose fermentation by the gut microbiota (fermentative dysbiosis), resulting in abdominal discomfort and diarrhea, the latter caused by the osmotic effects of lactose, glucose, and galactose in the colonic lumen (Deng *et al.*, 2015).

Although carbohydrates are a fundamental component of the human diet, providing a vital energy source alongside proteins and fats, studies have shown that certain individuals with fermentative dysbiosis are unable to adequately metabolize them, leading to the onset of gastrointestinal symptoms associated with malabsorption. Nutritional treatment is undoubtedly one of the indisputable aids capable of improving the clinical condition of patients, but dietary modification exposes these individuals to further alterations in microbiota biodiversity and potential nutritional deficiencies.

Recent studies have shown that the integration of probiotic bacteria, depending on their strain-specific actions, can be considered an important aid in modifying microbiota imbalances. This, in turn, contributes to the metabolism of carbohydrates such as fructans and lactose and enhances the bioaccessibility of micronutrients (Markowiak & Śliżewska, 2017).

Certain strain-specific probiotics, due to their biomodulatory capacity on the intestinal microbial ecosystem, can improve the state of hyperfermentative dysbiosis by reducing gas-producing species responsible for the clinical picture typical of carbohydrate malabsorption. Additionally, probiotics may mitigate the adverse effects of the Low-FODMAP Diet by promoting the absorption of micronutrients in

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the intestine, thanks to increased bioaccessibility of vitamins and minerals (Barkhidarian *et al.*, 2021).

The beneficial action of probiotics, particularly species belonging to the genus Lactobacillus, has been demonstrated through the genomic presence of gene loci responsible for lactose digestion and their actual production of beta-galactosidase, specific enzymes for the breakdown of this disaccharide (Ahn *et al.*, 2023).

Microbiota and non-celiac gluten/wheat sensitivity (NCGS/WS)

A specific category of food hypersensitivity is represented by disorders related to gluten ingestion, including celiac disease, wheat allergy, gluten ataxia, and non-celiac gluten/wheat sensitivity (NCGS/WS). Non-celiac gluten/wheat sensitivity (NCGS/WS) is a clinical condition characterized by intestinal and extra-intestinal symptoms triggered by gluten ingestion in the absence of wheat allergy (WA) or celiac disease (CD) (Calabriso *et al.*, 2022).

From a symptomatic perspective, individuals with this condition report intestinal disturbances such as transit alterations (constipation, diarrhea, or alternating bowel habits) associated with abdominal bloating. Many patients also describe sensations of postprandial fullness, gastroesophageal reflux, nausea, and extra-intestinal symptoms such as migraines, mood disturbances, anxiety and/or depression, as well as musculoskeletal manifestations. The clinical-symptomatic picture tends to improve upon gluten withdrawal from the diet and recurs following re-challenge (Caio G. *et al.*, 2020).

Gluten consists of a group of proteins, primarily prolamins and glutelins, found in cereals such as wheat (gliadins and glutenins), rye (secalins), and barley (hordeins). The abundance of glutamine and proline residues in gluten proteins reduces their degradation by human intestinal proteases, limiting their digestibility (Bascuñán *et al.*, 2020; Caio G. *et al.*, 2019).

In addition to gluten proteins, other wheat components have been associated with symptom onset, including alpha-amylase/trypsin inhibitors (ATIs), substances present in cereals as a defense mechanism against pathogens. Recent studies have demonstrated that ATIs exert an indirect effect on the human body by inhibiting the activity of gastrointestinal digestive enzymes and acting as anti-nutritional compounds capable of altering intestinal homeostasis and reducing the bioavailability of various micronutrients (Geisslitz *et al.*, 2021).

In sensitive individuals, these proteins can cause immune dysregulation. It has been demonstrated that gluten interacts with the intestinal epithelium through the CXC Motif Chemokine Receptor 3 (CXCR3), inducing the release of zonulin by en-

terocytes and allowing the passage of molecules from the intestinal epithelium into the *lamina propria*. Here, wheat proteins activate the innate immune system through Toll-like receptors (TLRs), particularly TLR-2 and TLR-4, inducing the release of pro-inflammatory cytokines.

Recently, in addition to gluten and ATIs, some authors have demonstrated a potential role of FODMAPs in the onset of symptoms reported by patients with NCGS/WS. Specifically, a randomized, double-blind, placebo-controlled study was conducted on 59 patients with NCGS/WS who reported gastrointestinal symptoms following gluten ingestion and were excluded from a diagnosis of celiac disease.

Patients were divided into three groups: the first group consumed 5.7 g of gluten daily for 7 days, the second group consumed 2.1 g of fructans daily, and the third group received a placebo for 7 days. After seven days of diet, patients in each group underwent a seven-day washout period until symptom resolution, followed by crossover to the next group until completing all trials (gluten, fructans, and placebo).

The study results showed that patients who consumed fructans experienced more gastrointestinal symptoms than those who consumed gluten or placebo. Specifically, fructan consumption led to a greater occurrence of abdominal pain, bloating, and bowel transit alterations, both constipative and diarrheal, compared to gluten and placebo, in a statistically significant manner (Skodje *et al.*, 2018).

Recent scientific evidence also suggests an important role of the gut microbiota in regulating innate immune responses in patients with NCGS/WS. It has been shown that the composition of the gut microbiota differs significantly in NCGS/WS individuals compared to healthy subjects, highlighting a state of marked intestinal dysbiosis.

The altered microbiota biodiversity is associated with increased expression of the TLR-2 receptor compared to healthy subjects. In NCGS/WS patients, intestinal dysbiosis correlates with significantly elevated serum levels of lipopolysaccharide-binding protein (LBP) and TLR-2, due to systemic immunity activation by the microbiota (Barbaro *et al.*, 2020; Dieterich *et al.*, 2019).

Currently, a gluten-free (GF) diet is considered the only effective treatment for patients with NCGS/WS. Although gluten exclusion significantly improves the clinical-symptomatic picture, this approach does not always guarantee complete symptom resolution due to patient compliance challenges and the risk of accidental gluten contamination.

Moreover, recent studies show that, in the medium to long term, the GF diet may negatively affect the biodiversity and richness of the intestinal microbiota, reducing beneficial species belonging to the genera *Lactobacillus, Bifidobacterium*, and *Faecalibacterium*, while favoring the growth of pro-inflammatory bacterial species from the *Enterobacteriaceae* family (Caio G. *et al.*, 2020). This can disrupt the intestinal microbial ecosystem, compromising intestinal homeostasis.

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As discussed, research has highlighted a state of intestinal dysbiosis in patients with NCGS/WS, exacerbated by the GF diet, despite its necessity for improving clinical symptoms. Evidence suggests that dysbiosis is linked to the reduced digestibility of wheat proteins, resulting in immune dysregulation and compromised intestinal barrier integrity.

This alteration of intestinal homeostasis, along with the GF diet, is responsible for the malabsorption of specific micronutrients, such as calcium (Ca), iron (Fe), magnesium (Mg), selenium (Se), potassium (K), copper (Cu), zinc (Zn), and vitamins (Skrypnik & Suliburska, 2018; Weyh *et al.*, 2022).

The role of probiotics in the malabsorption of carbohydrates and micronutrients

The growing body of scientific research in this field has demonstrated that strain-specific probiotic supplementation can promote intestinal homeostasis in these patients, primarily by countering intestinal dysbiosis and encouraging the colonization of beneficial bacterial species.

The continuous advancements in scientific research and the increased sensitivity of investigative techniques available today are enabling significant progress in understanding the functions performed by the intestinal microbiota and the role of probiotics in its modulation. This includes both compositional characteristics and the diverse metabolic activities attributed to it.

In recent years, the clinical application of probiotics has been garnering increasing interest within the scientific community to harness their potential molecular strategies. These aim to promote health-associated phenotypes and modulate disease-associated phenotypes. Probiotics are, in fact, regarded as microorganisms capable of contributing to the promotion of human health.

The Food and Agriculture Organization (FAO) of the United Nations and the World Health Organization (WHO) define probiotics as «live microorganisms which, when administered in adequate amounts, confer a health benefit on the host» (Hill *et al.*, 2014).

Numerous studies conducted both in vitro and in vivo, particularly using murine models, have identified specific molecular mechanisms that allow probiotic bacterial strains to exert their beneficial effects. These bacteria can secrete a vast number of molecules into the intestinal environment, acting as specific effectors in a complex interplay among the intestinal microbial ecosystem, immune cells, and intestinal epithelial cells.

Probiotic-derived effector molecules released into the intestinal lumen interact primarily with ecosystem components through cross-feeding interactions, altera-

tions of micro-environmental factors (e.g., pH modulation), competition for epithelial binding sites, and inhibition of pathogenic growth via the production of strain-specific antibacterial compounds. Probiotics also compete continuously for available nutrients within the intestinal environment (Lebeer *et al.*, 2010; Neeser *et al.*, 2000; Schiffrin & Blum, 2002; Verstrepen *et al.*, 2008).

Certain probiotic bacteria, thanks to their strain-specific modes of action, can synthesize specific enzymes (peptidases) targeting wheat proteins. They also exhibit antioxidant properties and contribute to the structural repair of intestinal villi.

Lactobacillus fermentum has demonstrated the ability to mitigate the damage associated with gluten ingestion by degrading gliadin peptides, thereby reducing their immunogenicity and structural damage to intestinal villi (Caminero *et al.*, 2019). Specifically, *Lactobacillus fermentum* has proven to be an effective probiotic in managing issues related to gluten ingestion, such as NCGS/WS, due to its ability to synthesize an x-prolyl dipeptidyl peptidase, known as PepX, with proteolytic activity specific to gluten proteins, particularly gliadin (Heydari *et al.*, 2023).

Furthermore, other studies have shown that *Lactobacillus fermentum* can degrade ATIs, significantly reducing their concentration by over 80% and consequently improving inflammatory parameters and intestinal epithelial damage caused by wheat ingestion (Caminero *et al.*, 2019).

As already emphasized, both individuals with carbohydrate malabsorption (FODMAP and lactose) and those with NCGS/WS often exhibit a pattern of micronutrient malabsorption, essential for their structural role and the many metabolic functions they perform. This deficiency is associated with several factors, including the dysbiotic and inflammatory state of the intestines, which causes an alteration of the intestinal epithelium, as well as adherence to dietary regimens that deprive them of essential food components.

Micronutrients play a crucial catalytic role for hormones, enzymes, and other bioactive components. They are directly linked to the proper functioning of the immune system, and their inadequate absorption influences susceptibility to infections and the development of chronic diseases such as neurodegenerative diseases, osteoporosis, and endocrine-metabolic diseases, including diabetes and thyroid disorders (Nath *et al.*, 2018; Steinbrenner *et al.*, 2022).

Research indicates that the level of minerals in the human body is primarily linked to their dietary intake. At the same time, the human body's functioning is tied not only to the quantity of minerals but also to their proportion and the percentage of absorption.

Recent studies show the direct involvement of the intestinal microbiota in mineral absorption through specific mechanisms that involve the complex interactions between microorganisms, minerals, and host cells (Peredo-Lovillo *et al.*, 2020). As

demonstrated by recent scientific evidence, an alteration in the biodiversity of the intestinal microbiota significantly impairs mineral absorption with systemic repercussions (Nath *et al.*, 2018).

Targeted probiotic supplementation may represent a complementary approach to addressing mineral deficiencies in individuals with poor intake or reduced absorption, as happens with a GF or LFD diet, or in other conditions such as gastroenteritis, colon diverticulosis, and gastrointestinal resections. Additionally, recent studies have shown that micronutrient malabsorption can also result from long-term pharmacological treatments (Karadima *et al.*, 2016).

Probiotics may offer a complementary approach to addressing mineral deficiencies in individuals with poor intake or absorption of minerals. By increasing the absorption and utilization of minerals, probiotics can counteract these deficiencies, which can have significant health implications. For example, probiotics have been considered for their potential role in improving the absorption of various minerals such as Ca, Se, Zn, Mg, and K. Adequate mineral absorption, especially Ca and Mg, is essential for maintaining optimal bone health to prevent conditions such as osteoporosis (Morato-Martínez *et al.*, 2020).

Probiotic bacteria, depending on their strain-specific action, are involved in mineral metabolism, improving absorption through specific mechanisms. It is important to note that the effects of probiotics on mineral absorption may vary due to many factors, including the specific probiotic strain, the dose and duration of probiotic supplementation, the presence of other nutrients or food components, and individual differences in intestinal microbiota (Bielik & Kolisek, 2021).

Specific probiotic bacteria, belonging to the Lactobacillus genus, can interact with minerals by producing enzymes capable of breaking down complex minerals, thereby making them more accessible for absorption by the host. These probiotic bacteria are among the major producers of phytase, a specific enzyme that our body cannot produce and is necessary for breaking down phytic acid, a compound present in many plant-based foods that can bind to minerals and prevent their absorption. By breaking down phytic acid, these probiotic bacteria can release minerals such as Fe, Ca, Mg, and Zn, making them available for absorption in the small intestine (Priyodip *et al.*, 2017; Scholz-Ahrens *et al.*, 2007; Zhou D. *et al.*, 2021).

Another potential mechanism by which probiotics can influence the bioavailability of minerals is the production of various metabolites resulting from probiotic fermentation of undigested carbohydrates. Among these are short-chain fatty acids (SCFAs: acetic acid, propionic acid, and butyric acid), which promote the solubility of minerals and improve the integrity of the intestinal epithelium.

Among the micronutrients crucial for human well-being, iron is certainly one of the most important. It is involved in oxygen transport, mitochondrial respiration,

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intermediary and xenobiotic metabolism, and cell growth and differentiation. However, today, iron malabsorption in the intestines is one of the most common nutritional problems, leading to an increased risk of iron deficiency in the human body. Iron deficiency is the leading cause of iron deficiency anemia and is associated with dysregulation of the host's immune response (Yilmaz & Li H., 2018). Several scientific studies have demonstrated how strain-specific probiotic supplementation can favor the intestinal luminal absorption of this micronutrient (Dje Kouadio *et al.*, 2024; González *et al.*, 2017; Zakrzewska *et al.*, 2022). In particular, metabolomic analysis of *Lactobacillus fermentum* has shown that it is a microorganism that produces hydroxyphenyl-lactic acid (HPLA), a bioactive metabolite with recognized antioxidant properties and an ability to increase the bioavailability of iron at the intestinal level.

In this regard, a recent study demonstrated that HPLA can promote the luminal intestinal absorption of iron. The mechanism through which HPLA acts is characterized by the reduction of Fe3+, the form typically found in food, into Fe2+, which is more bioavailable. Researchers have shown that hydroxyphenyl-lactic acid in the intestines performs an action similar to that of duodenal cytochrome B (DcytB), a human-origin protein that helps iron enter enterocytes in its reduced form through specific channels (Varvara & Vodnar, 2024).

Some probiotic bacteria can promote the increase of bioaccessibility for other minerals. In particular, the production of SCFAs can influence the absorption of minerals like Ca, improving the architecture of intestinal villi and thus increasing their absorptive surface area. SCFAs can also enhance the metabolism of this trace mineral by increasing the expression of calcium-binding proteins and its paracellular transport. Likewise, a high level of SCFAs can reduce the pH of the cecum and colon, improving mineral solubility. The reduction in pH leads to the dissolution of minerals and the easy release of Ca ions toward epithelial cells via the paracellular route, making it bioavailable for essential metabolic functions, such as the regulation of bone mineral density (Barkhidarian *et al.*, 2021; Beggs *et al.*, 2022; Li C. *et al.*, 2021; Zhou J. *et al.*, 2023). Studies have shown that some probiotics can improve the bioaccessibility and absorption of zinc (Zn). Specific probiotic bacterial strains can modulate the expression of specific proteins involved in its transport across the intestinal wall and contribute to the production of SCFAs, which, by reducing the intestinal pH, promote its solubility. Finally, the bioaccessibility of Zn can also be improved by biotransforming its inorganic form into an organic one, facilitating luminal intestinal absorption and thereby increasing serum levels, as recently demonstrated by researchers using Lactobacillus fermentum (Mohan *et al.*, 2018).

The mechanisms through which probiotics influence magnesium (Mg) absorption, actually, are not fully understood. Possible mechanisms of action may, as with

other micronutrients already discussed, relate to bacterial production of SCFAs that, by reducing intestinal pH, increase solubility. Some studies suggest that probiotics may improve the expression and activity of specific transport proteins, leading to increased Mg absorption. Finally, probiotics can favor the regulation of tight junction (TJ) proteins, thereby influencing the movement of magnesium ions and other micronutrients across the intestinal epithelium (Chamniansawat *et al.*, 2023; Tribst *et al.*, 2019).

Another trace element whose bioavailability can be influenced by an alteration in intestinal homeostasis (dysbiosis) is selenium (Se). This micronutrient is crucial for the function of certain enzymes called selenoproteins, such as glutathione peroxidase, iodothyronine deiodinase, and thioredoxin reductase, which are recognized for their important metabolic functions. These enzymes exert antioxidant action, capable of reducing the toxic effects of free radicals, decreasing cell death by apoptosis, and modulating thyroid function by contributing to the synthesis of thyroglobulin (TG) and thyroid hormones (T4, T3) (Bielik & Kolisek, 2021; Winther *et al.*, 2020).

As mentioned, the intestinal microbiota can influence selenium metabolism due to the overexpression of its own "selenoproteins". The bacterial species constituting our intestinal microbiota possess a variable number of selenoproteins that they use to ensure their optimal growth. Therefore, the intestinal microbiota, depending on its characteristic composition, can significantly influence the bioavailability of selenium for our organs and tissues.

Recently, some studies have demonstrated that the intestinal microbiota can influence the bioaccessibility, absorption, storage, and utilization of selenium by our cells, affecting the expression of SELP, the selenium transport protein. In conditions of altered microbiota biodiversity and chronic intestinal mucosal inflammation, SELP can undergo progressive down-regulation, preventing adequate absorption and transport of this trace element (Kasaikina *et al.*, 2011; Ramírez-Acosta *et al.*, 2022; Skalny *et al.*, 2025).

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