INTEGRATIVE REVIEW

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Probiotic supplementation in reducing exercise-induced gastrointestinal symptoms in endurance athletes: an integrative review

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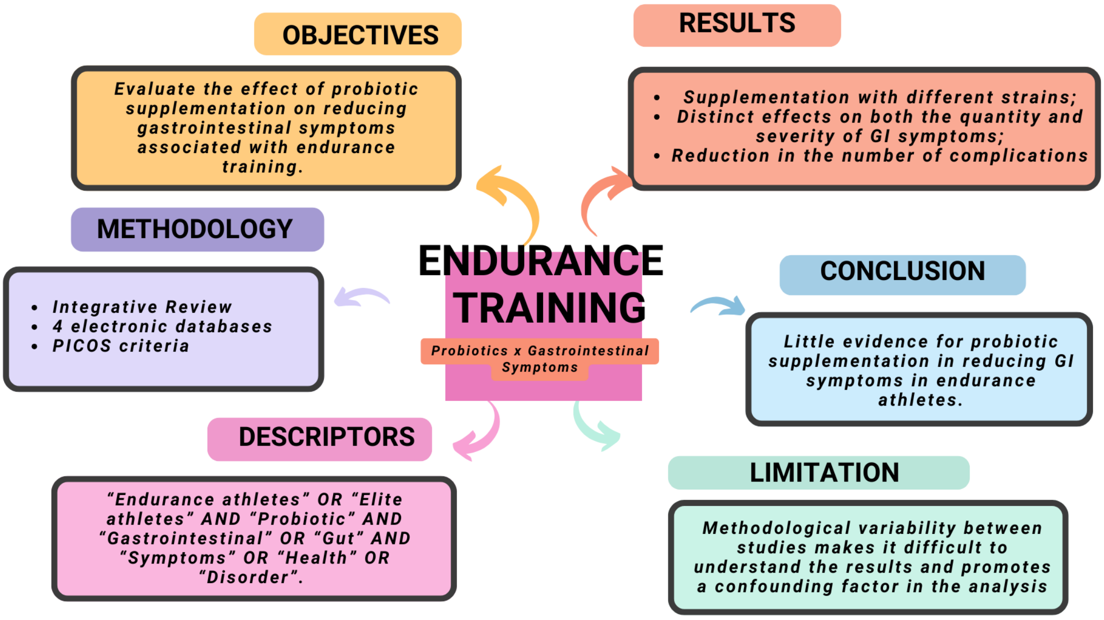
Graphical abstract

Highlights

- *Regular exercise improves gut microbiota diversity.*
- *Exercise-induced gastrointestinal syndrome affects athletes' performance and health.*
- *Probiotic supplementation may reduce the severity of gastrointestinal symptoms.*
- *Endurance training is associated with "exercise-induced gastrointestinal syndrome".*



Abstract

Endurance exercise can cause significant disturbances in the gastrointestinal tract, known as "exercise-induced gastrointestinal syndrome." These disturbances may lead to gastrointestinal symptoms and affect athletes' performance and health. This integrative review evaluated the effect of probiotic supplementation in reducing gastrointestinal symptoms associated with endurance exercise, discussing possible underlying mechanisms. The review was conducted in August 2024 across four electronic databases (PubMed, Scopus, Cochrane Library, ScienceDirect), using a search strategy based on the PICO criteria. The search terms included: "Endurance athletes" OR "Elite athletes" AND "Probiotic" AND "Gastrointestinal" OR "Gut" AND "Symptoms" OR "Health" OR "Disorder." Randomized controlled clinical trials involving adult endurance athletes were included. A total of 265 articles were identified, of which nine met the eligibility criteria. The interventions involved supplementation with various strains of probiotic bacteria and produced different effects in both the number and severity of GI symptoms during training periods, reducing the number of reported incidents among participants. Due to methodological differences among the studies, it was not possible to determine the best supplementation protocol. Most studies did not report promising outcomes regarding GI-related symptom parameters, yielding heterogeneous results. The methodological variability across studies hinders result interpretation and introduces confounding factors in the analysis. Thus, probiotic supplementation should be approached with caution, respecting GI symptoms and the individual response of each athlete.

Keywords: Probiotics. Athletes. Endurance Training. Gastrointestinal Tract. Gut Microbiota.

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INTRODUCTION

The gut of a healthy adult is characterized by a diverse community of microorganisms that symbiotically inhabit the digestive system, forming the gut microbiota, which plays an important role in many metabolic processes, such as the fermentation of undigested carbohydrates into short-chain fatty acids (SCFAs), lipid metabolism, and vitamin synthesis. It also contributes to the maturation of the immune system, protection against potentially pathogenic microorganisms, cognitive performance, and stress tolerance[1,2].

It is noteworthy that genetic and environmental factors, in addition to diet and antibiotic use, greatly influence the composition of the gut microbiota. New evidence suggests a plausible association between exercise and the composition of the gut microbiota[3,4,5,6,7].

It is known that regular training and exercise have been associated with changes in the composition and diversity of the microbiota, with an increase in SCFA content, especially butyrate, which serves as an energy source for intestinal epithelial cells; propionate, a precursor for glucose synthesis in the liver; and acetate, which is metabolized in muscle tissue[8]. Furthermore, SCFAs improve the integrity of the intestinal barrier, reducing the risk of local and systemic inflammation in individuals engaging in physical exercise[9,10].

On the other hand, prolonged strenuous exercise, such as in endurance disciplines, which are characterized by repetitive isotonic contraction of muscle groups and resistance to fatigue due to long periods of muscular activity[11], can lead to gastrointestinal (GI) disturbances due to potential epithelial damage. This damage increases intestinal permeability, causes endotoxemia, reduces nutrient absorption, and promotes inflammatory processes[12]. This set of disturbances, resulting from the stress induced by intense exercise, is known as "exercise-induced gastrointestinal syndrome" (EIGS), which is associated with symptoms in athletes such as belching, bloating, abdominal pain, regurgitation, abnormal stools, and nausea, impairing performance and causing health problems[13].

Probiotics, defined as "live microorganisms that, when administered in adequate amounts, confer a health benefit on the host"[14], have been used in supplement form to mitigate gastrointestinal symptoms caused by strenuous physical activity. They can alter the composition of the gut microbiota, increase microbial diversity, inhibit pathogen adhesion, enhance intestinal barrier function, and modulate the immune response[15,16,17,18,19,20]. The International Society of Sports Nutrition (ISSN) also suggests that certain probiotic strains may be used to reduce the severity of gastrointestinal infections[21]. In addition, some evidence demonstrates positive effects of probiotic supplementation on intestinal barrier function, inflammatory markers, and oxidative stress[22,23,24], indicating potential benefits for health maintenance and performance enhancement.

The effect of probiotic supplementation on athletic performance has been widely discussed in recent systematic reviews[23,25,26]. However, the results are heterogeneous, mainly due to methodological limitations in the studies analyzed, such as study design, strain variety and dosage, sample population, and performance measures used. Investigations into the effects of probiotics on the reduction of GI episodes or improvement of symptoms related to EIGS are less frequently reported in the literature[27].

In light of the above, this integrative review aims to evaluate the effect of probiotic supplementation on the reduction of exercise-induced gastrointestinal symptoms and to discuss the possible underlying mechanisms, with the goal of developing strategies to maintain performance and overall health in this population.

MATERIAL AND METHODS

This article consists of an integrative literature review, conducted in six stages: 1) identification of the topic and selection of the guiding research question; 2) establishment of inclusion and exclusion criteria and literature search; 3) definition of the information to be extracted from the selected studies; 4) categorization of the studies; 5) evaluation and interpretation of the studies included in the integrative review; and 6) presentation of the review.

The bibliographic search was conducted independently in August 2024 across four electronic databases: PubMed, Scopus, Cochrane Library, and ScienceDirect. The search strategy was developed based on the PICO criteria, using the Boolean operators "AND" and "OR," and was guided by the research question, as presented in Table 1.

Table 1 - Description of PICO Criteria, Guiding Research Question, and Search Terms Used, Curitiba, PR, Brazil, 2024.

Parameter	Description
Population (P)	Elite athletes; Endurance athletes
Intervention (I)	Probiotic supplementation
Comparison (C)	Placebo
Outcome (O)	Reduction of symptoms related to exercise-induced gastrointestinal syndrome (EIGS)
Guiding research question	"Can probiotic supplementation alleviate the events associated with exercise-induced gastrointestinal syndrome (EIGS) compared to placebo?"
Search strategy	"Endurance athletes" OR "Elite athletes" AND "Probiotic" AND "Gastrointestinal" OR "Gut" AND "Symptoms" OR "Health" OR "Disorder"

To select the articles resulting from the database searches, the following inclusion criteria were applied: a) intervention with probiotic supplementation only, without any other concurrent supplementation; b) randomized, placebo-controlled clinical trial; c) adult individuals practicing any endurance modality; d) comparison between groups with the same training level; e) evaluation of the intervention outcomes on gastrointestinal symptoms.

The exclusion criteria were as follows: a) use of other supplements or ergogenic substances; b) review articles, monographs, dissertations or theses, abstracts, book chapters, expert opinions or viewpoints; c) studies in which the outcome assessed was not related to endurance training/practice; d) sample population with comorbidities or diseases; e) intervention period shorter than four weeks.

The search results were exported from the databases to the reference management software Rayyan®. After removing duplicates, study selection was performed based on title and abstract screening, followed by full-text reading.

The articles included in the integrative review, based on the established inclusion criteria, proceeded to the data extraction phase, which included: author/year; study design; participant characteristics; intervention (strains, dosages, and protocols); control/placebo group; and study duration. Additionally, the reference lists of all selected studies were reviewed to identify any potentially relevant studies that may have been omitted.

Subsequently, using a pre-standardized form (Microsoft Excel®), the following data were extracted from the studies: authors, year of publication, study design, participant characteristics, sample size, supplementation protocol (strains, dosage, administration), and authors' conclusions.

RESULTS

Study selection

The search process across the selected databases identified a total of 265 articles: PubMed (n = 84), Scopus (n = 22), Cochrane Library (n = 8), and ScienceDirect (n = 151). A total of 220 articles were excluded due to duplicates (n = 41) or based on title and abstract screening (n = 179). Subsequently, 45 studies were assessed for eligibility, of which 39 were excluded for not meeting the established inclusion criteria, as follows: review articles (n = 21), no control group (n = 2), no analysis of gastrointestinal symptoms (n = 6), different modalities (n = 2), multiple supplementation (n = 1), acute intervention (n = 4), and other reasons (n = 3). At the end of the process, a total of 6 articles met the inclusion criteria and were included in the review. After reviewing the reference lists of the selected studies, 3 additional relevant articles were identified. The complete article selection flowchart for the integrative review is presented in Figure 1.

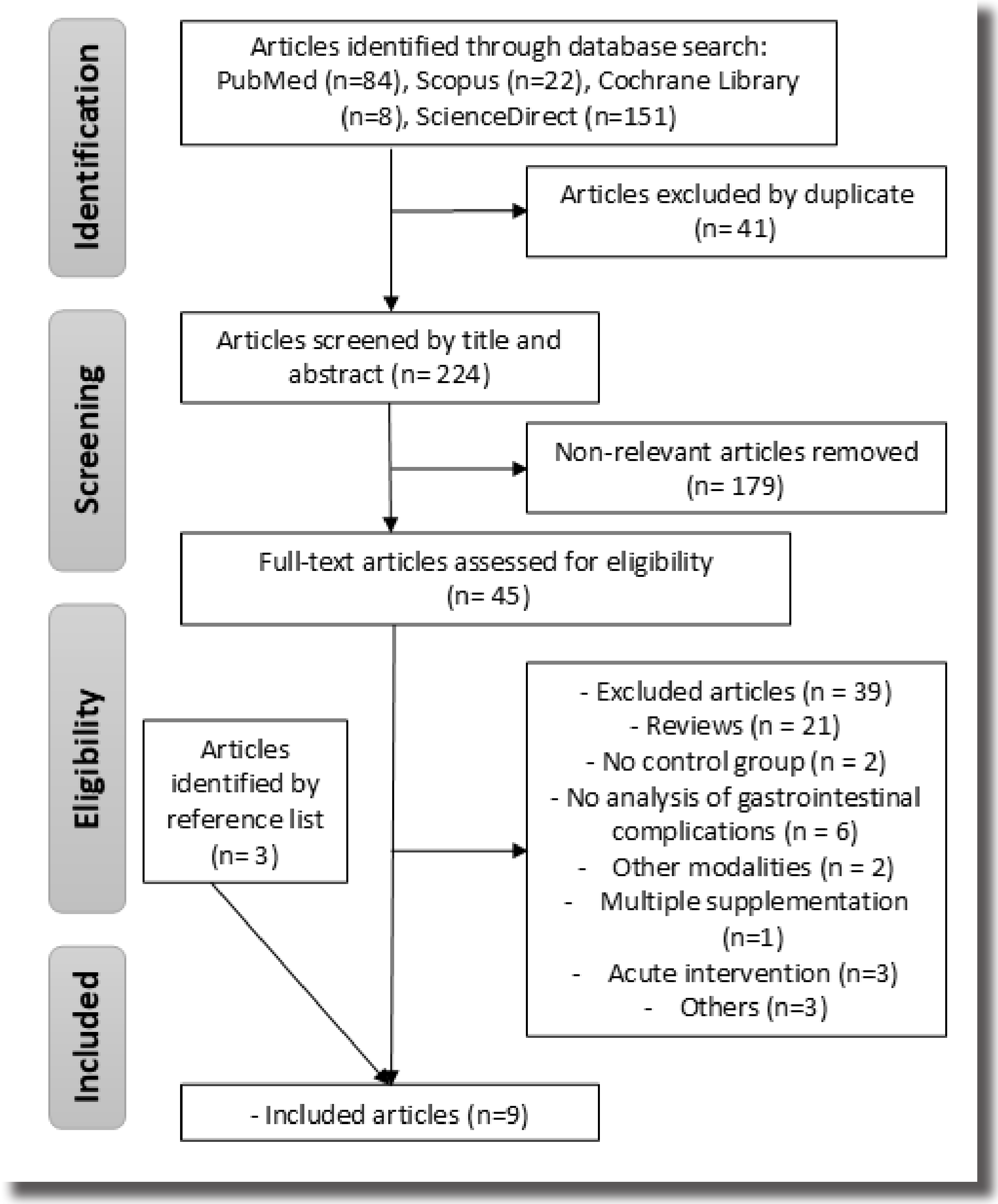

Figure 1 - Flowchart of the article search and selection process. Curitiba, Paraná, Brazil, 2024.
Sample and study characteristics.

The studies included a total of 488 participants (men = 376 and women = 112), with three studies recruiting only male participants[17,28,29], and six including both men and women[15,16,18,30,31,32]. Participant ages ranged from 18 to 69 years and consisted of recreational exercisers or endurance athletes in cycling, swimming, running, and triathlon disciplines. In most studies, supplementation was administered in capsule form[15,17,18,28,29,30,32], while some used beverages[30,31]. The interventions involved supplementation with various strains of probiotic bacteria such as *Bifidobacterium* and *Lactobacillus*. One study also used fructo-oligosaccharide[15]. Seven studies followed a parallel design[15,16,17,18,30,31,32], and two employed a crossover design[28,29]. Table 2 presents the characteristics of the articles, including: author/year; study design; participant characteristics; intervention (strains, doses, and protocols); control/placebo group; and study duration.

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Table 2 - Characteristics of the articles selected for integrative review. Curitiba, PR, Brazil, 2024.

Author (year)	Study Design	Participant Characteristics	Intervention (strains, dose, protocol)	Control/Placebo Group	Study Duration
Kekkonen *et al.* (2007)[30]	Double-blind, randomized, parallel clinical trial	Marathon runners; men (n = 125) and women (n = 16); 22–69 years	Capsule or fruit-based milk drink (65 mL); single strain: *Lactobacillus rhamnosus* (3×10^8 CFU/mL; 5×10^9 CFU/capsule); 2x/day	Capsule or fruit-based milk drink (65 mL); 2x/day	12 weeks
Gleeson *et al.* (2011)[31]	Double-blind, randomized, parallel clinical trial	Endurance trainees; men (n = 54) and women (n = 30); 18–55 years	Fermented milk container (65 mL); single strain: *Lactobacillus casei* (6.5×10^9 CFU/container); 2x/day	Fermented milk without probiotic (65 mL); 2x/day	16 weeks
West *et al.* (2011)[32]	Double-blind, randomized, parallel clinical trial	Cyclists and triathletes; men (n = 64) and women (n = 35); 35 years (M), 36 years (F)	Capsule; single strain: *Lactobacillus fermentum* (1×10^9 CFU/capsule); 1x/day	Capsule; microcrystalline cellulose; 1x/day	11 weeks
Shing *et al.* (2014)[28]	Double-blind, randomized, crossover clinical trial	Runners; men (n = 10); 27 years	Capsule; multiple strains: *L. acidophilus*, *L. rhamnosus*, *L. casei*, *L. plantarum*, *L. fermentum*, *B. lactis*, *B. breve*, *B. bifidum*, *S. thermophilus*; 1x/day	Capsule; skim milk powder; 1x/day	4 weeks
Roberts *et al.* (2016)[15]	Double-blind, randomized, parallel clinical trial	Endurance trainees; men (n = 25), women (n = 5); 35 years	Capsule; multiple strains: *L. acidophilus* (2×10^{10} CFU), *B. bifidum*, *B. lactis* (1×10^{10} CFU); 1x/day	Capsule; corn flour (200 mg); 1x/day	12 weeks
Pugh *et al.* (2019)[16]	Double-blind, randomized, parallel clinical trial	Runners; men (n = 20), women (n = 4); 22–50 years	Capsule; multiple strains: *L. acidophilus*, *B. bifidum*, *B. lactis* (2.5×10^{10} CFU); 1x/day	Capsule; corn starch; 1x/day	4 weeks
Pugh *et al.* (2020)[29]	Double-blind, randomized, crossover clinical trial	Cyclists; men (n = 7); 23 years	Capsule; multiple strains: *L. acidophilus*, *B. bifidum*, *B. lactis* (2.5×10^{10} CFU); 1x/day	Capsule; starch; 1x/day	4 weeks
Schreiber *et al.* (2021)[17]	Double-blind, randomized, parallel clinical trial	Elite cyclists; men (n = 27); 19–40 years	Capsule; multiple strains: *L. helveticus*, *B. lactis*, *E. faecium*, *B. longum*, *B. subtilis*; 1x/day	Capsule; excipients: potato starch, magnesium stearate, ascorbic acid, white vegetable powder; 1x/day	13 weeks
Smarkusz-Zarzecka *et al.* (2022)[18]	Double-blind, randomized, parallel clinical trial	Long-distance runners; men (n = 46), women (n = 20); 20–60 years	Capsule; multiple strains: *B. lactis*, *L. brevis*, *L. case*i, *Lc. lactis*, *L. acidophilus*, *B. bifidum*, *L. salivarius* (2.5×10^9 CFU/capsule); 2x/day	Capsule; no probiotic bacteria; 1x/day	12 weeks

Regarding the parameters used by the authors related to gastrointestinal symptoms, a detailed analysis was conducted to illustrate the results and assess the magnitude of the effect of probiotic supplementation during training and competition periods (during and after). The parameters analyzed were: number of GI symptoms, proportion of individuals with symptoms, severity, duration of symptoms, and intestinal barrier function. The results are presented in Table 3.

Table 3 - Impact of probiotic supplementation on gastrointestinal (GI) symptoms and intestinal barrier function during training, competition, and post-competition periods. Curitiba, PR, Brazil, 2024

Author	Number of GI symptoms	Proportion of individuals with GI symptoms (%)	GI symptom severity	Symptom duration (days)	Intestinal barrier function
Impact of probiotics on GI symptoms during training					
Kekkonen *et al.* (2007)[30]	↔	↔	-	↔	-
Gleeson *et al.* (2011)[31]	-	↔	↔	↔	-
West *et al.* (2011)[32]	↑	-	↓	↑	
Roberts *et al.* (2016)[15]	↓	-	↓	-	↔
Pugh *et al.* (2019)[16]	↓	-	-	-	↔
Schreiber *et al.* (2021)[17]	↓	-	-	-	-
Smarkusz-Zarzecka *et al.* (2022)[18]	↔	↔	-	-	-
Impact of probiotics on GI symptoms during competition					
Shing *et al.* (2014)[28]	↔	-	-	-	↔
Pugh *et al.* (2019)[16]	-	-	↓	-	↔
Pugh *et al.* (2020)[29]	-	-	↔	-	↔
Impact of probiotics on GI symptoms after competition					
Kekkonen *et al.* (2007)[30]	↔	↔	-	↓	-
Pugh *et al.* (2019)[16]	-	-	-	-	↔
Schreiber *et al.* (2021)[11]	-	-	↔	-	-

Caption: ↓ significant reduction of effect, ↔ no significant effect, ↑ significant increase of effect.

Number of GI Symptoms and Proportion of Individuals with GI Symptoms (%)

Six studies assessed the number of gastrointestinal (GI) symptoms[15,16,17,18,28,32], with five of them evaluating symptoms during training periods. Only one study assessed this parameter during a fatigue test session[28].

Three articles in the review showed positive effects of probiotic supplementation on the number of GI symptoms experienced by participants in the intervention groups compared to placebo[11,16,17]. However, two studies did not observe significant effects in reducing GI symptoms between the intervention and placebo groups, although they reported that the duration of a GI symptom episode was 57% shorter in the probiotic group (1 day vs. 2.3 days)[18,30].

Conversely, one article reported an increase in the number of self-reported mild GI symptoms (low severity) among participants taking probiotics[32].

Three studies assessed the proportion of individuals who experienced GI symptoms during training or after competition, with no significant differences observed between the probiotic and placebo groups[18,30,31].

Severity and Duration of GI Symptoms

Six articles analyzed the effects of probiotics on the total severity score of gastrointestinal symptoms[15,16,17,29,31,32], of which three assessed changes during training[15,31,32] and two during competition or sports events[16,29]. Post-competition analysis was conducted in only one study[17].

Two studies showed significant reductions in symptom severity scores during training using multiple strains (*Lactobacillus acidophilus* (2 × 10^{10} CFU/capsule)), *Bifidobacterium bifidum* and *Bifidobacterium lactis* (1 × 10^{10} CFU/capsule) and a single strain (Lactobacillus fermentum (1 × 10^{9} CFU/capsule))[15,32]. Only one article reported positive effects during competition, and only at the end of a marathon, using a multi-strain formulation (*L. acidophilus*, *B. bifidum*, *B. lactis* (2.5 × 10^{10} CFU/capsule))[16]. In contrast, three studies did not observe significant effects on severity scores during training (single strain: Lactobacillus casei (6.5 × 10^{9} CFU/container))[31], during competition (multi-strain: *L. acidophilus*, *B. bifidum*, *B. lactis* (2.5 × 10^{10} CFU/capsule))[33], or after sports events (multi-strain: *L. helveticus* (4.3 × 10^{9} CFU/capsule), *B. lactis* (4.3 × 10^{9} CFU/capsule), E. faecium (3.9 × 10^{9} CFU/capsule), B. longum (2.1 × 10^{9} CFU/capsule), and B. subtilis (0.4 × 10^{9} CFU/capsule))[17].

Three articles evaluated the duration of gastrointestinal symptoms during training[30,31,32], presenting mixed results. Two studies found no significant differences in symptom duration between the probiotic and placebo groups (capsule or fruit-based milk drink (65 mL) – single strain: *Lactobacillus rhamnosus* (3 × 10^{8} CFU/mL; 5 × 10^{9} CFU/capsu-

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le), and single strain: *L. casei* (6.5 × 10^9 CFU/container))[30,31]. One study, however, observed that the duration of mild GI symptoms was longer among participants consuming the probiotic (*L. fermentum* (1 × 10^9 CFU/capsule))[32]. Additionally, only one study reported positive effects on reducing GI symptom duration, specifically two weeks after competition (*L. rhamnosus* (3 × 10^8 CFU/mL; 5 × 10^9 CFU/capsule))[30].

It is worth noting that in most studies evaluating gastrointestinal symptoms primarily abdominal bloating, nausea, urge to vomit, flatulence, urge to defecate, and stomach cramps symptoms were scored using a visual analog scale from 0 to 10. When multiple symptoms were present, they were classified as "moderate" and/or "severe," while fewer symptoms were classified as "mild." This approach made it difficult to compare and individually describe symptoms associated with probiotic use across different interventions.

Intestinal Barrier Function

Four articles evaluated changes in intestinal barrier function with probiotic supplementation[15,16,28,29]; however, no statistically significant differences were observed between the study groups.

DISCUSSION

Endurance athletes are exposed to strenuous and prolonged exercise and frequently experience gastrointestinal symptoms, affecting between 30% and 90% of individuals depending on personal factors, duration, intensity, and type of endurance training[34]. The most common symptoms include belching, nausea, regurgitation, reflux, bloating, abdominal pain, intestinal discomfort, and diarrhea, which may impair athletic performance and lead to chronic health problems[33].

This integrative review investigated the effects of probiotic supplementation on gastrointestinal events related to EIGS during training and competition periods in various groups of athletes, mostly runners, cyclists, swimmers, and triathletes. The findings revealed discrepancies in the magnitude of probiotic effects across different parameters analyzed in the studies, possibly due to methodological differences.

In the findings of the present review, probiotic interventions showed significant effects on both the frequency and severity of GI symptoms during training periods, reducing the number of reported events and the degree of severity with which they occurred[15,16,17,32], according to the questionnaires.

In these studies, supplementation involved both single and multi-strain formulations, including *Lactobacillus fermentum* (1 × 10^9 CFU/capsule)[32], *Lactobacillus acidophilus* (2 × 10^{10} CFU/capsule)[9] and (2.5 × 10^{10} CFU/capsule)[16], *Bifidobacterium bifidum* (1 × 10^{10} CFU/capsule)[15] and (2.5 × 10^{10} CFU/capsule)[16] and (4.3 × 10^9 CFU/capsule), *Bifidobacterium lactis* (1 × 10^{10} CFU/capsule)[15], (2.5 × 10^{10} CFU/capsule)[16], *Lactobacillus helveticus* (4.3 × 10^9 CFU/capsule)[17], *Enterococcus faecium* (3.9 × 10^9 CFU/capsule)[17], *Bifidobacterium longum* (2.1 × 10^9 CFU/capsule)[17], and *Bacillus subtilis* (0.4 × 10^9 CFU/capsule)[17]. Similarly, recent reviews demonstrate that probiotic supplementation appears to influence the prevention of GI episodes and the reduction of symptoms induced by intense physical exercise[35,36].

The observed benefit is possibly due to the positive effects of probiotics on GI health and their role in regulating intestinal homeostasis[14,18]. They act through four main mechanisms: 1. production of antimicrobial substances; 2. antagonism against pathogen adhesion to the intestinal epithelium and competition for nutrients; 3. modulation of immune function; 4. improvement of intestinal barrier function and nutrient absorption[37,38]. Together, these physiological mechanisms help reduce exercise-induced endotoxemia and inflammation, which may in turn decrease gastrointestinal events[19].

Kekkonen *et al.* (2007)[30] observed significant reductions in the duration of GI symptom episodes with *Lactobacillus rhamnosus* supplementation compared to the placebo group, during the two-week period following competition. *L. rhamnosus* exerts regulatory effects on intestinal homeostasis and the immune system, suggesting a positive impact in combating intestinal infections[39]. Conversely, West *et al.* (2011)[32] reported that the duration of mild, self-reported GI symptoms during training was twice as long in the group supplemented with *Lactobacillus fermentum*. However, this increase may be explained by short-term adaptations in the GI tract due to the introduction of new bacterial species and changes in fermentation activity[40].

Endurance training promotes blood flow redistribution away from the GI tract (splanchnic hypoperfusion) and alters the activity of the enteric nervous system, triggering a cascade of GI events[41]. These physiological responses can disrupt and compromise intestinal integrity, negatively affecting permeability, barrier function, and systemic responses[13,42]. Once epithelial fragility is established, bacterial translocation increases, resulting in higher levels of endotoxemia and inflammatory processes factors that may lead to GI symptoms[13].

Although improvement in intestinal barrier function with probiotic supplementation has been suggested due to its potential to defend against exercise-induced endotoxemia and inflammation[42], the evidence analyzed in this review does not support this effect, as no significant differences were found in barrier function following probiotic use.

One explanation for the discrepancy in results regarding the parameters analyzed across studies is the methodological variability, particularly in relation to the supplementation protocols used (doses, strains, forms of administration). Probiotics have strain-specific differences in their ability to colonize the GI tract, clinical efficacy, and the type and magnitude of associated health benefits[43]. Investigating the same outcome while using different forms of supplementation complicates the consistency of findings.

Diet is an intrinsically related factor in alterations of the gut microbiota, given the wide nutritional variety present in foods. Aspects such as macronutrient type, intake of fermented foods, dietary fiber, high sugar and fat consumption, and abrupt changes in dietary intake can influence microbiota function[44]. A balanced intake of different nutrient types and quantities positively affects the bacterial community and its diversity, whereas an unbalanced diet can contribute to the development and progression of disease[45]. The lack of dietary control in the studies reviewed may represent a confounding factor in the results, since, like probiotics, the intake of specific nutrients can alter gut bacterial populations and produce significant changes.

To reduce bias regarding probiotic supplementation and gastrointestinal symptoms, future research should standardize supplementation protocols (strains and dosage) and implement stricter dietary control during the intervention period. It is also important to monitor the use of carbohydrate-based supplements and nutritional strategies during competition periods, as these are common practices in endurance sports[46].

This review presents important limitations that must be considered when interpreting the findings. There is methodological variation among the included studies in terms of participant characteristics (age, sex, training level), strains used (proportion, dosage, frequency), and intervention duration. The use of different supplementation protocols, varied methods for identifying GI symptoms, and the lack of dietary control contribute to difficulties in interpreting results. Additionally, the small sample sizes limit statistical power and may confound the identification of significant effects. Conclusions should therefore be interpreted within the context of these limitations.

CONCLUSION

The integrative review found limited evidence supporting the use of probiotic supplementation to reduce GI symptoms in endurance athletes during training and competition, indicating low effectiveness as a nutritional strategy. Most studies did not present promising outcomes regarding the evaluated GI symptom parameters, with heterogeneous results. The methodological variability among studies hinders result interpretation and introduces confounding factors into the analysis. Therefore, the limited evidence does not support the use of probiotics as a supplement for athletes aiming to alleviate exercise-induced GI symptoms. The scarcity of well-designed and controlled studies highlights the need for further research to clarify the impacts of probiotic supplementation on GI events in athletes and to enable more conclusive findings on the subject.

CRediT author statement

Project Administration: Andreoli RVT; Bertin RL. Formal Analysis: Andreoli RVT; Bertin RL. Conceptualization: Andreoli RVT; Bertin RL. Data Curation: Andreoli RVT; Bertin RL; Ulbrich AZ. Writing – Original Draft: Andreoli RVT; Bertin RL. Writing – Review & Editing: Andreoli RVT; Bertin RL; Ulbrich AZ. Investigation: Andreoli RVT; Bertin RL. Methodology: Andreoli RVT; Bertin RL; Ulbrich AZ.

All authors have read and agreed to the published version of the manuscript.

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.

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