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USE OF SYNBIOTICS FOR THE TREATMENT OF DYSBIOSIS AND THE CONSEQUENT IMPLICATIONS ON PHYSICAL PERFORMANCE

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ABSTRACT
Synbiotics are composed of live microorganisms that can bring benefits to the individual's health, consisting of the aggregation between prebiotics and probiotics, indicated for favoring the development of beneficial microorganisms for intestinal regulation, among the functions, there is the increased resistance of the strains against pathogens. Intestinal dysbiosis is a process of colonic dysfunction due to an imbalance in the intestinal microbiota, as pathogenic bacteria are prominently beneficial. Therefore, with the imbalance, the microbiota favors the growth of microorganisms that produce toxins that are absorbed into the bloodstream, causing inflammatory processes. The present study is a systematic review of the literature with the characteristic of exploratory research, with the initial question being based on and determined by the PICO method with the selection of studies in the virtual search carried out by publications indexed in the database: *Latin American and Caribbean Literature in Health Sciences*, *US National Library of Medicine* and *Scientific Electronic Library Online*element. The inclusion criteria for scientific articles should be original, randomized, controlled clinical trials published between 2015 and 2020. To assist in this situation, intense physical exercise implies adaptive processes that involve physiological, biochemical and cognitive-behavioral responses, in an attempt to recover homeostasis. When prolonged, intense physical exercise is associated with a transient depression of immune function in athletes, while moderate exercise beneficially influences the immune system. The level of physical activity contributes as a protection against the presence of dysbiosis, with beneficial repercussions on the composition of the gut microbiota. Synbiotics stand out as essential compounds to promote health benefits by helping in the passage of fecal bolus during evacuation, contributing to the restructuring of the intestinal mucosa and, thus, preventing the appearance of intestinal discomfort, common in the process of dysbiosis.

Keywords: Symbiotics. Dysbiosis. Exercise.

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INTRODUCTION

Synbiotics are composed of live microorganisms that can bring benefits to the individual's health, consisting of the aggregation between prebiotics and probiotics, indicated for favoring the development of beneficial microorganisms for intestinal regulation, promoting an action with greater clinical efficacy, therefore, symbiotic supplementation is attracting the attention of the sports community to promote health and exercise performance (Tsutsumi, *et al*, 2011; Araújo, 2016).

Among the functions of synbiotics, there is mainly the increased resistance of strains against pathogens, thus, the modulation of the intestinal microbiota by probiotic microorganisms occurs through the mechanism of "competitive exclusion" and the strains that beneficially influence are *Bifidobacterium bifidum, Lactobacillus rhamnosus, Sacharomyces boulardii* and *Lactobacillus plantarum* (Souza, *et al*, 2010).

These strains associated with galactooligosaccharides and fructooligosaccharides (prebiotics) become the main compounds that confer benefit to gastrointestinal health. In addition, it favors the passage of the fecal bolus during evacuation, restructuring the intestinal mucosa and, consequently, prevents the appearance of intestinal discomfort, characteristic of dysbiosis (Tsutsumi, *et al*, 2011; Reis, Ribeiro, 2019).

Intestinal dysbiosis is a process of colonic dysfunction due to an imbalance in the intestinal microbiota, since pathogenic bacteria are prominently beneficial. Therefore, with the imbalance, the microbiota favors the growth of microorganisms that produce toxins that are absorbed into the bloodstream, causing inflammatory processes (Almeida, *et al*, 2010).

It also promotes an increase in the number of bifidobacteria, beneficial microorganisms present in the intestinal microbiota, glycemic control, reduction of blood cholesterol levels, balancing of the healthy intestinal microbiota that helps reduce constipation and/or diarrhea, improvement of intestinal permeability and stimulation of the immune system, essential factors for maintaining health and the proper practice of physical performance (Reis, Ribeiro, 2019).

Intense physical exercise implies adaptive processes that involve physiological, biochemical and cognitive-behavioral responses, in an attempt to recover homeostasis. When prolonged, intense physical exercise is associated with a transient depression of immune function in athletes, while moderate exercise beneficially influences the immune system (Nieman, *et al*, 2011).

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Although there are already studies associating microbiota and physical exercise, this relationship is not yet well understood (Estaki, *et al*, 2016). Recent studies suggest that the gut microbiota may play a key role in controlling oxidative stress and inflammatory responses, as well as improving metabolism and energy expenditure during intense exercise. However, the relationship between exercise-induced stress and gut microbiota composition, as well as the possible pathophysiological mechanisms involved, have not yet been explored (Lambert, *et al,* 2015; Pyne, *et al*, 2015; Mach, Fuster-Botella, 2017).

The investigation of the association between intestinal modulation and probiotics in sports practice is relatively recent, yet studies in animal models and humans indicate that these microorganisms can be used to improve immune and gastrointestinal parameters and, consequently, performance (Clancy, 2010; Mcfadzean, 2014).

In view of the growing incidence of dysbiosis in physical exercisers, causing gastrointestinal discomfort that impairs performance in performance, it is suggested to investigate what would be the physiological mechanism of action of the synbiotics that ensure the homeostasis of the organism?

It is understood that in view of the current situation, it is essential to guarantee the needs and prevent or combat intestinal complications, a detrimental factor for physical performance, and it is necessary to analyze the appropriate support for these individuals, following the literature. In this context, the objective of the present study was to analyze the use of synbiotics for the treatment of dysbiosis and, consequently, the implications for the physical performance of endurance practitioners.

METHODOLOGY

The present study is a systematic review of the literature with the characteristic of exploratory research, in which the initial question was based on and determined by the PICO method, which represents an acronym for patient, intervention, comparison and *outcomes* (Santos, Pimenta Nobre, 2007), therefore, referring to the question about From dysbiosis in practitioners of physical exercise, causing gastrointestinal discomfort that impairs performance in performance, it is suggested to investigate what would be the physiological mechanism of action of the synbiotics that guarantee the homeostasis of the organism.

For the development of this study, six (06) steps were outlined: I) identification of the theme and formulation of the guiding question; II) establishment of the criteria for

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inclusion/exclusion of articles; III) search in the existing literature; IV) cataloguing of studies; V) analysis of the results; VI) synthesis of findings and preparation of the manuscript.

The strategy of identification and selection of studies in the virtual search was carried out by publications indexed in the database: LILACS (*Latin American and Caribbean Literature on Health Sciences*), PUBMED (*US National Library of Medicine*) and SCIELO (*Scientific Electronic Library Online*), during the month of August 2020.

In the process of virtual search for articles, the Boolean operator (AND) was used in the association of the following descriptors: "Symbiotics". Physical exercise", and "Dysbiosis". The evaluation of the eligibility criteria was independently prepared by the reviewers (authors).

As inclusion criteria, scientific articles should be original, available in full, and randomized controlled clinical trials, published between 2015 and 2020, in English, Portuguese, and Spanish, excluding duplicate articles, theses, and monographs.

Initially, the articles were submitted to an eligibility evaluation by reading the titles and abstracts, excluding those that had no correlation with the proposed theme, then a complete reading of the manuscripts was carried out, rigorously analyzing their methods and conclusions. This step was carried out by independent reviewers who declared that there was no disagreement with the selected articles.

The abstracts of the selected articles were analyzed to verify whether they corresponded to the inclusion criteria, such as presenting a controlled clinical trial design with the purpose of verifying the use of synbiotics for the treatment of dysbiosis and the consequent implications on physical performance.

Subsequently, a survey of information and data extraction was carried out, including the type of study, objectives, duration of the study, methods and/or interventions adopted, characteristics of the population studied, clinical setting, analysis of results, main outcomes and conclusions. The data were ordered and tabulated in the Electronic Spreadsheet of *Microsoft Office Excel for Windows 2007*. The organization consisted of: authors, year of publication, database, title of the article, objective, methodology, results, and conclusion.

The interpretation of the data and the synthesis of the collected information occurred through a critical analysis, according to the main objective of the study, seeking scientific evidence to analyze the use of synbiotics for the treatment of dysbiosis and, consequently, the implications on the physical performance of endurance practitioners.

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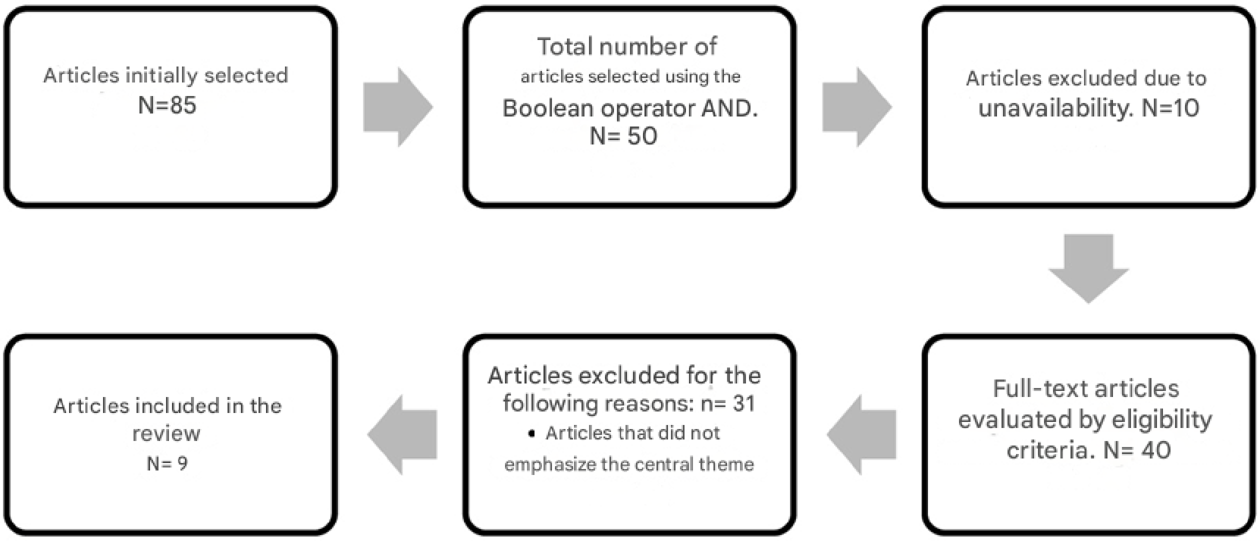
From the material obtained, there was a detailed reading of each article used for the construction of the study, highlighting those who responded to the proposed objective, in order to organize and tabulate the data.

The production of this article followed the guidelines of the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) protocol, which corresponds to a *checklist* with 27 items to assess risks of bias in the inclusion of articles and a flowchart consisting of 04 steps: identification, screening, eligibility and inclusion (Shamseer, *et al*, 2015).

RESULTS

Of the 85 articles identified, the part found for the results of the study were from LILACS. In this identification stage, 76 articles (89%) were excluded because they were articles that did not address the central theme of the study, thus, the remaining 9 articles served as a basis for the construction of this study due to their relevance and that corresponded to the research objectives, after applying the research criteria (Figure 01).

Figure 01: Flowchart of the stages of selection, inclusion and exclusion of articles in the databases.



The sample of articles for the discussion of the central theme of the study consists mainly of 9 main and relevant articles, selected by the previously established inclusion criteria, in Chart 1 are the specifications of the main articles for the elaboration of the discussion.

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The information extracted from the selected studies is presented in Chart 01.

Table 1: Summary of selected articles

AUTHORS/YEAR/ DATABASE	GOAL	METHODOLOGY	MAIN RESULTS	CONCLUSIONS
Moreira, *et al* (2019)	To verify the anthropometric profile and prevalence of signs and symptoms suggestive of intestinal dysbiosis in bodybuilders in the municipality of Picos.	This is a cross-sectional, descriptive, quantitative study, involving bodybuilders in gyms, of both sexes. Weight and height were obtained to obtain the Body Mass Index (BMI).	Most were within normal weight for both sexes, 53.3% of men and 58.2% of women had high results for body fat. Most of them had a low risk of developing cardiovascular diseases according to the waist-to-hip ratio, and visceral fat was also adequate. It was found that the values that did not indicate the presence of hypersensitivity corresponded to 47.1%, and 41.4% showed the presence of hypersensitivity.	The results suggested the presence of gut dysbiosis in exercisers.
Jardim, *et al.* (2018)	To identify the prevalence of hypersensitivity and intestinal dysbiosis in military police officers through the metabolic screening questionnaire.	A cross-sectional study was carried out with military personnel from a battalion stationed in São Luís, sociodemographic information was collected and a metabolic screening questionnaire was applied.	The sample consisted of 40 men, with a mean age of 39.9±8.3 years, most of whom were married and had higher education. According to the screening score, 55.1% were healthy, and the prevalent gastrointestinal symptom was heartburn (57.5%). There was a low presence of hypersensitivity among the military personnel, but gastrointestinal symptoms, such as heartburn, constipation, related to dysbiosis were found in a significant portion of the military personnel·.	Therefore, the symptoms must be monitored, as the imbalance of the bacterial flora can cause damage to their health.
Caldeira, Ferreira, Ferreira. (2018)	OBJECTIVE: To analyze the prevalence of dysbiosis in a group of obese and eutrophic individuals practicing physical exercise.	This is a cross-sectional, exploratory and descriptive study, applying questionnaires with university students, presenting objective questions in order to observe possible changes in the functioning of the intestinal microbiota, and physical exercise, thus being associated with nutritional status.	No discrepant differences were found in the scores of the intestinal hyperpermeability questionnaire in relation to exercise practice and BMI. Although the BMI scores were not so discrepancies, the overweight and obese group deserves attention, since they were classified as mild and moderate treatment priority for intestinal hypermeability.	It suggests a higher risk of dysbiosis, and it is important to apply therapy that uses prebiotics and probiotics that will modulate the intestinal microbiota.
Jacobine. (2019)	To evaluate the relationship between intestinal dysbiosis and the level of physical activity in Nutrition students from a university center in the interior of Pernambuco	This is a cross-sectional study with a quantitative approach, involving 100 participants. Data regarding signs and symptoms were quantified using the Metabolic Screening Questionnaire (MRQ)	The prevalence of signs and symptoms of dysbiosis was found in 11% (n=11) of the university students, who obtained a score ≥10 in the gastrointestinal tract section of the MRQ,	The level of active physical activity, presented by most of the students of the Nutrition Course evaluated, seems to contribute as a protection against the

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			which characterizes them with dysbiosis.	presence of dysbiosis, with beneficial repercussions on the composition of the intestinal microbiota of university students.
Dantas, *et al*. (2017)	To evaluate the prevalence of gastrointestinal symptoms during national triathlon competition.	The study included 11 amateur triathletes, of both sexes, age (33.3 ± 8.5 years), body mass (76.8 ± 9.1 kg men and 60.1 ± 4.4 kg women), who answered a questionnaire about the presence of upper and lower gastrointestinal tract symptoms during the competition.	. There are several etiological factors involved in the appearance of gastrointestinal symptoms during exercise, such as intestinal hypoperfusion, endotoxemia, dehydration, dietary and mechanical factors, in addition to aspects related to exercise.	The triathletes evaluated presented several gastrointestinal symptoms, predominantly of the upper gastrointestinal tract.
West, *et al*. (2015)	To examine the effect of probiotic supplementation on respiratory and gastrointestinal diseases in healthy, active men and women.	A randomized, double-blind, placebo-controlled trial was conducted. Four hundred and sixty-five participants (241 males and 224 females) were divided into one of three groups: Group 1 Bifidobacterium animalis subsp. lactis Bl-04 (Bl-04) 2.0 × 10 (9) colony-forming units per day, CFU per day, Group 2 - Lactobacillus acidophilus NCFM and Bifidobacterium animalis subsp. lactis Bi-07 (NCFM & Bi-07) 5 × 10 (9) CFU each per day) or Group 3 – placebo.	The risk of an episode of upper respiratory disease was significantly lower in the Bl-04 group (hazard ratio 0.73; 95% confidence interval 0.55-0.95; P = 0.022) compared to placebo. There was no significant difference in disease risk between the NCFM and Bi-07 group (hazard ratio 0.81; 0.62-1.08; P = 0.15) and the placebo group. There was a delay of 0.7 and 0.9 months in the median time to one episode of illness in the Bl-04 and NCFM and Bi-07 groups, respectively, compared to placebo (placebo 2.5 months; Bl-04 3.2 months; NCFM and Bi-07 3.4 months).	The probiotic Bl-04 appears to be a nutritional supplement useful in reducing the risk of URIs in physically active healthy adults.
Roberts, *et al*. (2016)	To evaluate the impact of a multistrain pro/prebiotic/antioxidant intervention on endotoxin unit levels and GI permeability in recreational athletes.	Thirty healthy participants were assigned and assigned to a multistrain pro/prebiotic/antioxidant (LAB^4_{ANTI}; 30 billion CFU·day^{-1} containing 10 billion CFU·day^{-1} *Lactobacillus acidophilus* CUL-6, 10 billion CFU·day$-^1$ *Lactobacillus acidophillus* CUL-21 (NCIMB 30156), 9.5 billion CFU·day$-^1$ *Bifidobacterium bifidumCUL-20 (NCIMB 30172) and 0.5 billion CFU· day* $^{-1}$ *Bifidobacterium animalis* subspecies *lactis* CUL-34 (NCIMB 30153) /55.8 mg · day $^{-1}$ fructooligosaccharides / 400 mg · day $^{-1}$ α-lipoic acid, 600 mg · day $^{-1}$ *N* -acetyl-carnitine); paired pro/prebiotic or placebo (PL) for 12 weeks prior to a long-distance triathlon.	Endotoxin unit levels were not significantly different between groups at baseline ($LAB^4_{ANTI:}$ 8.20 ± 1.60 pg · mL $^{-1}$; LAB ^{4} : 8.92 ± 1.20 pg.mL $^{-1}$; PL: 9.72 ± 2.42 pg · mL $^{-1}$). The use of a $^{12\text{-week}}$ $_{LAB\,4}$ ANTI intervention significantly reduced endotoxin units both pre-run (4.37 ± 0.51 pg · mL $^{-1}$) and six days after running (5.18 ± 0.57 pg · mL $^{-1}$; *p* = 0.03, ηp ^{2} = 0.35), but only six days after running with LAB ^{4} (5.01 ± 0.28 pg · mL $^{-1}$; *p* = 0.01, ηp ^{2} = 0.43). In contrast, endotoxin units remained unchanged with PL. L:M increased significantly from 0.01 ± 0.01 at baseline to 0.06 ± 0.01 with PL alone (*p* = 0.004, ηp ^{2} = 0.51). Average running times (h:min:s) were not statistically different	The combined use of multistrain pro/prebiotics can reduce endotoxin unit levels, with LAB^4_{ANTI} potentially conferring an additive effect through combined GI modulation and antioxidant protection.

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			between groups, despite faster times with both pro/prebiotoic groups.	
Huang, *et al.* (2020)	To investigate how the microbiota of triathletes is altered by *L. plantarum*.PS128 supplementation, not only for exercise performance, but also for possible physiological adaptation	The triathletes were divided into two groups: a *L. plantarum* 128 supplement group (LG, 3 × 10 [10] colony-forming units (CFU)/day) and a placebo group (GP). Both groups continued with their regular exercise training for the next 4 weeks. The endurance performance, body composition, biochemistry, blood cells, microbiota and associated metabolites were further investigated.	PS128 significantly increased the endurance of the athletes, by about 130% compared to the PG group, but there was no significant difference in maximal oxygen uptake (VO_{2max}) and composition between the groups. Supplementation with PS128 (LG) modulated the athlete's microbiota with significant decreases in the strains characteristic of a dysbiosis process and increased effective regulation	PS128 supplementation was associated with an improvement in endurance running performance through modulation of the microbiota and related metabolites, but not in maximal oxygen consumption.
Strasser, *et al.* (2016)	To examine the effect of a probiotic supplement on the incidence of upper respiratory tract infections (URTIs) and aromatic amino acid metabolism after exhaustive aerobic exercise in athletes trained during three months of winter training.	Thirty-three highly trained subjects were randomly assigned to either probiotic (PRO, *n*=17) or placebo (PLA, *n*=16) groups using double-blind procedures, receiving 1 × 10 [10] colony-forming units (CFU) of a multi-species probiotic (*Bifidobacterium bifidum* W23, *Bifidobacterium lactis* W51, *Enterococcus faecium* W54, *Lactobacillus acidophilus* W22, *Lactobacillus brevis* W63, and *Lactococcus lactisW58) or placebo once daily for 12 weeks.*	After 12 weeks of treatment, post-exercise tryptophan levels were reduced by 11% (a significant change) in the PLA group compared to concentrations measured before the intervention (*p*=0.02), but remained unchanged in the PRO group. The proportion of subjects taking placebo who experienced one or more symptoms of URIs increased 2.2-fold compared to those receiving probiotics (PLA 0.79, PRO 0.35; *p*= *0.02).*	Data indicate reduced rates of exercise-induced tryptophan degradation in the PRO group. Daily supplementation with probiotics limited exercise-induced drops in tryptophan levels and reduced the incidence of URTIs, however, it did not benefit athletic performance.

DISCUSSION

From the analysis of the articles, it is possible to observe aspects related to the appearance of gastrointestinal symptoms and hypersensitivity during the practice of physical exercise, in addition to the administration of probiotics and synbiotics correlated with better physical performance, body mass index (BMI) and the probability of developing chronic non-communicable diseases.

Regarding the prevalence of gastrointestinal symptoms in physical exercisers, it was observed in an observational and cross-sectional study that the majority (75%) of the sample was composed of men, between 27 and 49 years of age, and the minority of women (25.0%), between 29 and 43 years of age. Of the 14 symptoms reported, 78.6% were related to the upper gastrointestinal tract and only 21.4% related to the lower gastrointestinal tract, with heartburn and gas being the most prevalent symptoms (36.0%), followed by lateral pain present in 21% of the sample and some of the amateur triathletes reported more than one symptom, thus, the total frequency of symptoms was greater than the number of people (Dantas, *et al*, 2017).

While the increased risk of dysbiosis is found in studies to observe changes in the functioning of the gut microbiota during physical exercise. Thus, it evaluated a group of individuals who practice exercise, investigating cases of mild and moderate intestinal hypermeability, causing the following symptoms during training: stomach pain, indicating a symptom of esophageal reflux characterized as epigastric pain, in addition to gas, diarrhea and nausea, demonstrating marked intestinal irregularities during the physiological process of physical exercise (Caldeira, Ferreira, Ferreira, 2018).

Thus, when there is an imbalance in the intestinal microbiota caused by the increase in the number of harmful bacteria, the practice of physical activity is one of the factors responsible for provoking physiological responses, resulting from autonomic and hemodynamic adaptations that positively influence the gastrointestinal tract during physical exercise. It has been demonstrated in cross-sectional research on the relationship between intestinal dysbiosis and physical activity, finding the prevalence of signs and symptoms of dysbiosis in 11% of the participants and having a significant association between the practice of physical activity and dysbiosis, as 92% of active individuals do not have dysbiosis, while in those classified as inactive only 76% did not have dysbiosis (Jacobine, 2019).

The level of physical activity contributes as a protection against the presence of dysbiosis, with beneficial repercussions on the composition of the intestinal microbiota, in addition, the need for synbiotic supplementation is perceived to assist and intensify this process of recovery of the healthy microbiota. It was observed in a randomized double-blind placebo-controlled trial, divided into three groups: the 1st group had supplementation of Bifidobacterium animalis subsp. lactis, the 2nd had supplementation of Lactobacillus acidophilus and Bifidobacterium animalis, and the 3rd group had the placebo mixed in a drink. In this case of supplementation, there were no reports of insufficient gastrointestinal tract symptoms for the study, compared to the placebo group (West, *et al*, 2015; Dantas, *et al,* 2017).

CONCLUSION

Synbiotics stand out as essential compounds to promote health benefits by helping in the passage of fecal bolus during evacuation, contributing to the restructuring of the intestinal mucosa and, thus, preventing the appearance of intestinal discomfort, common in the process of dysbiosis.

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In addition to stimulating the increase of bifidobacteria, beneficial microorganisms in the intestinal microbiota, promoting glycemic control that reduce blood cholesterol levels, balancing healthy intestinal microbiota and improving intestinal permeability that, in this way, strengthen the immune system to maintain health and optimize physical performance.

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