



Review article

Probiotics and sports: A new magic bullet?

Geovana S.F. Leite Ph.D. Student ^{a,*}, Ayane S. Resende Master Student ^a, Nicholas P. West ^b, Antonio H. Lancha Jr ^a

^a Laboratory of Nutrition and Metabolism Applied to Motor Activity, School of Physical Education and Sports, University of Sao Paulo, Sao Paulo, Brazil

^b Menzies Health Institute Queensland and School of Medical Science, Griffith University, Griffith Health Gold Coast Campus, Southport, QLD, Australia



ARTICLE INFO

Article History:

Received 12 July 2018

Accepted 29 September 2018

Keywords:

Probiotics

Athletes

Sports

Exercise

Immune response

Gastrointestinal tract

ABSTRACT

The use of probiotics in sports has been growing in the past years focusing on the attenuation of upper respiratory tract (URS) and gastrointestinal (GI) symptoms commonly present in endurance athletes. Researches shown different results and this may related to the probiotic strain, dose, period consumption or even the form of administration (capsules, sachets or fermented milk). These four factors directly influence in the probiotic's outcome and this question still remains unclear. Thus, the goal of this review is to clarify how these factors may influence the outcomes, approaching the major differences among studies, mechanisms by which the probiotic may contribute in sports field and applied conclusions. It was used 'probiotics', 'athletes', 'sports', 'exercise', 'athletes performance', 'immune response', 'intestinal symptoms' as keywords and its combinations and 20 original articles were selected for our purpose. All the articles were performed in healthy physically active people and/or athletes. Putting together, it was observed that athletes may benefit from probiotics consumption. It seems that multi strain ingested via sachet or fermented food and a larger period of consumption may shown better results at minimizing URS and GI symptoms. Also, specific species appears to have a role in exercise recovery. Therefore, the beneficial effect of probiotics in sports field is strictly dependent on the four factors abovementioned. The molecular mechanisms behind the probiotics effectiveness have not yet been elucidated and perhaps the biological assessments performed in the studies as well the few number of studies published did not answer the question yet.

© 2018 Elsevier Inc. All rights reserved.

Introduction

In sports it is known that athletes may be at risk of several disorders as a result of an exhaustive training load, exercise intensity, travel, inadequate rest, and poor nutrition [1,2]. Strenuous exercise promotes immunodepression, oxidative stress, increased upper respiratory illness symptoms (URS), and gastrointestinal (GI) disorders [3,4]. Moreover, especially athletes in long distance sports (marathon, triathlon, and ultra-endurance) commonly report health issues and endotoxemia [1,5,6]. Thus there is a growing body of investigators looking for strategies, especially in the nutritional supplementation field, to prevent these conditions from affecting sport performance [4].

Antonio H. Lancha participated in the conception of this review; Geovana S. F. Leite and Ayane S. Resende were involved the design and development; Nicholas P. West performed the revision of the manuscript critically for important for intellectual content. The figure and table were constructed by Geovana S. F. Leite and Ayane S. Resende. All authors read and approved the final manuscript.

* Corresponding author. Tel.: +55(11)30913096.

E-mail address: geovana.leite@usp.br (G.S.F. Leite).

In this context, probiotic supplementation has gained special attention because of evidence of a beneficial effect on respiratory and gastrointestinal tract symptoms [1,7,8]. The beneficial effects of probiotics may indirectly influence the performance of athletes by preventing illness negatively affecting performance [9]. Probiotics are considered a well-tolerated treatment to use in athletes; however, it is difficult to reproduce study outcomes with athletes around the world. Perhaps the various results found may be from different interventions, such as use of different probiotics strains or multistrains and time and dose of consumption, along with the use of different athletic cohorts [8,10,11]. Currently there is no consensus about whether probiotics may have an ergogenic effect or improve recovery beyond improving resistance to infectious and non-infectious agents that underpin illness conditions. In this sense the goal of the present review is to examine the main mechanisms by which probiotics can contribute to sport performance and the major differences among the interventions that interfere in outcomes. Our focus is on the main benefits and practical issues of probiotics consumption concerning immune response, gut disorders, and athletes' performance.

Probiotics consumption in the sports environment: Evidence for efficacy

Immune health in athletes

Heavy training periods or a heavy schedule of competitions increase the risk of illness, in particular URS, in athletes. URS include coughing, congestion, sneezing, sore throat, and mucus production. The risk of illness is considered acutely greater in the immediate postexercise period, a phenomenon termed the “open window” hypothesis. Evidence strongly indicates that in this window there is decreased host protection with reduced NK cell number and activity, low neutrophils activity, impaired proliferation of T lymphocytes, and decreased levels of salivary immunoglobulin A (IgA) [8,12,13], which contributes to virus and bacteria being able to establish infection and cause illness.

Exercise immunology studies have reported that declines in salivary IgA precede upper respiratory illness episodes and symptoms in athletes [13,14]. Recurrent URS, particularly during heavy training, may affect athletic performance depending on the severity of illness symptoms and the requirement to alter training. The most likely causes of compromised immune activity are increased serum levels of contraregulating hormones cortisol and catecholamine produced during vigorous exercise [13]. Several points are linked with this phenomenon, such as poor nutrition strategies during and after the training session, lower micronutrients and macronutrient intake, insufficient recovery time, and an exhaustive high-level competition schedule. Together these issues contribute to increasing contraregulating hormones and consequently driving immune perturbations [4,15].

Probiotic supplementation and athlete health

A body of evidence supports that some probiotic supplements may attenuate the risk of URS or reduce the duration and severity of symptoms in athletes. Some studies also indicate that probiotics may alter serum cytokine concentrations and maintain salivary IgA concentrations (Table 1). A pivotal study by Clancy et al. [16] provided early evidence of a role for probiotics in modifying the immune system. This study investigated the relationship of *Lactobacillus acidophilus* (2×10^{10} per 4 wk) in recreational athletes with fatigue who exhibited a decrease in interferon- γ (IFN- γ) production by CD4 blood cells (compared with non-fatigued athletes). The authors found that after *L. acidophilus* consumption, both healthy and fatigued athletes exhibited an increase in IFN- γ production by T cells and non-fatigued athletes exhibited an increase in salivary IFN- γ concentration. The findings of this study suggest that baseline immune status may dictate responses to probiotic supplementation.

A number of studies have examined the effect of probiotics on URS. Cox et al. [17] conducted a study with a specific probiotic strain (*L. fermentum*) in highly trained runners. This consumption was capable of reducing the number of day symptoms of URS with a trend toward a lower severity of illness. West et al. [18], in a study with the same probiotic strain used by Cox [17] with minor dosage adjustments and a longer period application, found that after the intervention men had decreased URS and women had increased symptoms. Moreover, this report presented data related to cytokine response after the exercise that was modified by probiotic use [18]. The cytokines increased less after acute exercise in the intervention group. This may be the result of better immune regulation associated with *L. fermentum* supplementation. Nonetheless, Kekkonen et al. [19] found a modest increase in IgA and

IFN- γ in the probiotic group, but no statistically significant difference was found with use of *L. rhamnosus* GG (40×10^9 CFU/d).

Gleeson et al. [7], in work with well-trained endurance athletes consuming fermented milk containing the commercial available probiotic *L. casei* Shirota during a longer period of use (4 mo), found that the URS and episodes were lessened in the probiotic group (Table 1). Also, salivary IgA production was higher in the probiotic group after 8 and 16 wk of intervention. This study highlights that a benefit from probiotics in endurance athletes would be useful.

West et al. [20], in research with physically active participants rather than athletes, compared a monostrain and double strains of probiotics (Table 1). The results indicated that the monostrain *Bifidobacterium lactis* resulted in a 27% reduction in URS compared with placebo, whereas the double-strain probiotic resulted in a 19% non-significant decrease of URS risk. This study found for the first time that healthy active people, generally considered at the lowest risk of URS, could benefit from a probiotic supplement.

Haywood et al. [11] conducted an interesting study with probiotics in rugby players using a higher dose multispecies probiotic (4 wk). All the participants in the placebo group reported more URS than the probiotic group, although the duration and severity of the upper respiratory illness episodes and symptoms were not different between groups; however, the number of illness days in placebo groups trended higher compared with treatment [11].

Strasser et al. [15], with a similar multistrain probiotic to that used by Lamprecht [21], reported that this commercial multispecies probiotic is capable of reducing URS. Participants who had more symptoms had higher degradation of tryptophan and kynurenine-to-tryptophan ratios during the exercise. After probiotic intervention the probiotic group had a smaller decrease in tryptophan concentration after exercise compared with placebo. These data confirm the efficacy of the probiotic in attenuating the URS.

According to a study by Michalickova et al. [22] with long-term use of capsules containing *L. helveticus* Lafti L10 in high concentration (2×10^{10} CFU/d), this probiotic was effective to reduce the length of episode and the number of URS. Similar result were reported by Cox et al. [17] and West et al. [18] with use of *L. fermentum* VRI-003 (PCC) and Gleeson et al. [7] with fermented milk containing *L. casei* Shirota. Moreover an increase in CD4-to-CD8 ratio was found in the probiotic group. These authors suggested that low CD4-to-CD8 ratio is normally related to acute viral diseases and an improvement in this immunologic parameter could contribute to the favorable effects of Lafti L10 on URS.

Specific probiotics strains attenuate URS [17,18,22]; however, the data with non-athlete participants are quite small, and no alterations in cellular activity were found to explain the reduction of URS in the probiotic group [22]. Perhaps looking for immune cells function may contribute to clarify the decrease of illness symptoms and severity. Also, local modulation and interaction warrant attention, such as the use of saliva (e.g., IgA, lysozyme, α -amylase) and feces (zonulin, short chain fatty acids [SCFAs], α_1 -antitrypsin, occludins, IgA) measures as analytical material. Although the majority of studies monitored the dietary supplementation used by athletes, there is no sufficient information about participant consumption. This is valid information that can contribute for future works to discuss and justify the results.

Gut health and permeability

GI disorders are often reported in different situations in athletes, mainly in endurance sports. For instance, Pugh et al. [6] found that 249 athletes in several sports had at least one symptom (86% reported), varying between mild and moderately severe, and that

Table 1
Studies related to probiotic use in sports

Reference	Participants	Probiotics	URS outcomes		GI outcomes		Further considerations
			Subjective	Biological	Subjective	Biological	
Active individuals 20	Health active participants (n = 465)	Sachets containing 2×10^9 <i>Bifidobacterium lactis</i> ssp. <i>lactis</i> BI-04 or double strain (<i>Lactobacillus acidophilus</i> NCFM 5×10^9 and <i>B. animalis</i> ssp. <i>lactis</i> Bi-07 5×10^9 UFC/d for 5 mouths	<i>B. lactis</i> was effective to reduce the URS episodes compared with placebo and Bi-07	NR	24% reduction in risk of illness in both probiotics groups compared with placebo	NR	RDBCP Placebo group and Bi-07 group had different level of physical activities (intensity and duration) 8 individuals presented some type of GI illness, with majority in the probiotics groups (7 vs. 1 placebo)
Athletes 16	Recreational athletes: healthy athletes, n = 18; fatigued athletes, n = 9 (male/female)	Capsules containing 20×10^9 CFU/d <i>L. acidophilus</i> LAFTI L10 for 4 wk	Fatigued athletes present more episodes of upper respiratory illness/year and lost more activities related to it	Before probiotic use, fatigued athletes had decreased of IFN- γ production by CD4 compared with non-fatigued athletes After probiotic use, fatigued athletes exhibited increased IFN- γ production by CD4 cells, and non-fatigued athletes exhibited increased salivary IFN- γ	NR	NR	Both groups received the intervention. Fatigued athletes (20.9 h) had higher training volume compared with non-fatigued (10.7 h)
19	Marathon runners (n = 119)	Milk-based fruit drink containing <i>L. rhamnosus</i> GG (40×10^9 CFU/d) for 3 mo	<i>L. rhamnosus</i> GG had no effects related to URS incidence compared with placebo	NR	Duration of GI symptoms was 33% shorter during the training period and 57% shorter 2 wk after the marathon in the probiotic group	NR	RDBCP Probiotic consumption varied the quantities (1×10^{10} and 4×10^{10} /per day) and type of administration No significant difference in GI illness episodes between groups Study was conducted during a summer training period RDBCP
17	Elite male runners athletes (n = 20)	Capsules containing <i>L. Fermentum</i> VRI-003 (PCC) 12×10^9 CFU/d for 4 wk	Probiotic group presented a reduction in number of days with illness symptoms	Probiotics group presented a modest increase in IgA and IgA1 salivary concentration but no statistical significance was found A modest increase in IFN- γ production was found in	NR	NR	Runners who participated of the study competed in

(continued on next page)

Table 1 (Continued)

Reference	Participants	Probiotics	URS outcomes		GI outcomes		Further considerations
			Subjective	Biological	Subjective	Biological	
18	Competitive cyclists (male = 64/female = 35)	Capsules containing <i>L. fermentum</i> VRI-003 (PCC) 1×10^9 CFU/d for 11 wk	For male participants the probiotics were effective by decreasing URS	probiotic group without statistical significance The cytokines released after acute exercise were attenuated in probiotic group	Lower severity score of GI symptoms in men in the probiotic group at high training loads	Increase of 330% of <i>Lactobacillus</i> genus numbers in the probiotic group with a 7.7-fold difference between groups	events from 800 m to marathons (42.2 km) The study was conducted during a winter training period RDBCP Study was conducted during the winter training period Intervention results were different between men and women Probiotic group reported 2 times more mild GI illness episodes (number and duration) than placebo group RDBCP
7	Endurance athletes (n = 58) (male/female)	Fermented milk containing <i>L. casei</i> Shirota 6.5×10^9 CFU/2 times per day during 16 wk	Placebo group had significantly more URS and episodes compared with probiotic group	Salivary IgA concentration was higher after 8 and 16 wk of probiotics intervention Placebo group had decreased IgA concentration during the study	NR	NR	Study was conducted during training period; the mean training hour/wk was 10 h. The fermented milk was ingested together with breakfast (first) and in the evening(second) RDBPC
35	Endurance athletes (n = 66) (male/female)	Sachets containing <i>L. salivarius</i> , 2×10^9 CFU/d during 16 wk	No difference in URS duration between groups	No difference related to IgA salivary level Probiotic group had increased lymphocyte totals after the intervention	NR	NR	Similar to Gleeson [7] RDBCP
21	Male athletes (n = 23)	1×10^{10} CFU/d of a multi-species (<i>B. bifidum</i> W23 + <i>B. lactis</i> W51 + <i>E. faecium</i> W54 + <i>L. acidophilus</i> W22 + <i>L. brevis</i> W63 + <i>Lactococcus lactis</i> W58) in a sachet with a matrix* for 14 wk	NR	NR	NR	Significant reduction of zonulin concentrations in probiotic group	No differences in α -antitrypsin concentrations Study included triathletes, runners, and cyclists (continued on next page)

Table 1 (Continued)

Reference	Participants	Probiotics	URS outcomes		GI outcomes		Further considerations
			Subjective	Biological	Subjective	Biological	
11	Elite rugby players ($n = 30$)	Capsules containing <i>L. gasseri</i> 2.6×10^9 <i>B. bifidum</i> 2.6×10^9 <i>B. longum</i> 2×10^8 CFU/d for 4 wk	Probiotic group reported less URS during intervention	NR	Significantly lower presence of GI symptoms after probiotic consumption	NR	Crossover design This study was conducting during a winter training period Crossover design
24	Male runners ($n = 10$)	45×10^9 CFU/d of a multi-species (<i>L. acidophilus</i> + <i>L. rhamnosus</i> + <i>L. casei</i> + <i>L. plantarum</i> + <i>L. fermentum</i> + <i>B. lactis</i> + <i>B. brevis</i> + <i>B. bifidum</i> + <i>S. thermophilus</i>) in capsules for 4 wk	NR	NR	NR	Significant lower plasma LPS concentration after probiotic consumption compared with baseline Moderate reduction in GI permeability in probiotic group	endotoxemia
10	Endurance male runners ($n = 8$)	Beverage containing <i>L. casei</i> 1×10^{11} CFU/d during 1 wk	NR	No difference in cytokine profile in probiotic group after intervention	NR	No effect on	Probiotic group had a trend of increased inflammatory parameters after intervention RDBCP
14	Recreational athletes (male = 155/ females = 113)	Fermented milk containing <i>L. casei</i> Shirota 6.5×10^9 CFU/2 \times per day during 5 mo	No differences related to URS, number of episodes, and duration of illness	The level of IgG-specific antibodies for cytomegalovirus (CMV) and Epstein-Barr virus in probiotic group was lower after intervention compared with baseline of the same group	NR	NR	Fermented milk was ingested together with breakfast (first) and in the evening meal (second) Participants in sports such as triathlon, swimming, cycling, distance running, tennis, squash, badminton, football, rugby, hockey, lacrosse, and basketball self-reported training loads of 11 h/wk RDBPC
22	Athletes ($n = 39$)	Capsules containing <i>L. helveticus</i> Lafti L10 2×10^{10} CFU/d for 14 wk	The number of URS were fewer and duration of episodes of illness were shorter in probiotic group, and they	Probiotic group had increases in CD4/CD8 T lymphocyte ratio after intervention	NR	NR	RDBPC

(continued on next page)

Table 1 (Continued)

Reference	Participants	Probiotics	URS outcomes		GI outcomes		Further considerations
			Subjective	Biological	Subjective	Biological	
25	Recreational triathletes (n = 30) (males/females)	2 × 10 ¹⁰ CFU/d of <i>L. acidophilus</i> + 9.5 × 10 ⁹ CFU/d of <i>B. bifidum</i> 0.5 × 10 ⁹ <i>B. animalis</i> ssp. <i>lactis</i> + 55.8 mg/d FOS in capsules during 12 wk	NR	NR	GI symptom episodes were lower in the probiotic + FOS group at each month of pre-race training, and the severity of GI symptoms was lower	Reduction in plasma endotoxin levels at pre-race and 6 d postrace (~26%), as well as for IgG levels recorded 6 d postrace Also, probiotics + FOS group had a lower increase in GI permeability compared with other groups	Athletes modalities: badminton, triathlon, cycling, alpinism, athletics, karate, savate, kayak, judo, tennis, and swimming Participants were instructed to take capsules every day after breakfast Athletes had a mean of 11 h/wk training RDBCP
15	Endurance athletes (n = 30)	Sachet with a matrix* containing 1 × 10 ¹⁰ CFU multi-species <i>B. bifidum</i> W23 + <i>B. lactis</i> W51 + <i>E. faecium</i> W54 + <i>L. acidophilus</i> W22 + <i>L. brevis</i> W63 + <i>Lactococcus lactis</i> W58) for 3 mo	Probiotic group had fewer URS after treatment	After the acute exercise, probiotic group had less decreased tryptophan level	NR	NR	There was a group with probiotic + FOS + α-lipoic-acid and <i>N</i> -acetyl-carnitine hydrochloride, but better overall outcomes were reported for the probiotic + FOS group (LAB ⁴) RDBCP Female participants had higher degradation of tryptophan compared with male participants Probiotic group had more training time per week compared with the placebo group

FOS, fructo-oligosaccharide; IFN, interferon; Ig, immunoglobulin; LPS, lipopolysaccharide; NR, not reported; RDBCP, randomized, double-blind, controlled, parallel groups design; URS, upper respiratory illness symptoms

*Matrix consisted of cornstarch, maltodextrin, vegetable protein, MgSO₄, MnSO₄, and KCl.

upper abdominal discomfort, flatulence, and urgent need to defecate were most common.

As opposed to moderate regular exercise, physical and psychological stress produced by both a high training load and exercise intensity cause disruption in the intestinal epithelium and barrier function. Hyperthermia and redistribution of blood flow causing ischemia and hypoperfusion in the intestinal environment, as well as the overstimulation of hypothalamic-pituitary-adrenal axis, are examples of exercise-induced stimuli [3]. This gut barrier is crucial for preventing the translocation of pathogenic bacteria and endotoxins, such as lipopolysaccharides (LPSs). The increase in gut permeability favors the translocation of LPS and bacteria into the intestinal system and bloodstream, which can result in endotoxemia [23]. For instance, endurance athletes often present elevated plasma LPS concentrations, and the majority may have endotoxemia [5,23].

Currently there are few studies that have evaluated the effect of probiotics on gut permeability and endotoxemia (Table 1). However, these studies have reported positive outcomes, with a significant reduction of fecal zonulin concentrations [21] and plasma endotoxin concentrations [24,25]. Interestingly, these studies used a multistrain probiotics supplement containing the species *L. acidophilus*, *B. bifidum*, and *B. animalis* ssp. *lactis* for at least 1 mo [21,24,25]. It is also believed that chronic interventions with longer periods of probiotic consumption are better for intestinal benefits because Gill et al. [10] did not identify an effect on endotoxemia with 1 wk of *L. casei* consumption [10].

Moreover, the majority of studies performed with this population have had better results in improvement of GI symptoms, mainly regarding severity, episodes, and duration (Table 1). Some studies did not find statistical differences between probiotic and placebo groups [18]. Still, athletes have reported clinical improvements, especially regarding the severity of these symptoms in training periods [11,19,25]. *Lactobacillus* and *Bifidobacterium* species, especially *L. acidophilus*, *L. rhamnosus* GG, and *B. bifidum*, seem to be interesting with regard to improving exercise-induced GI symptoms.

Probiotics also interact with the resident gut microbiota and may affect their composition. West et al. [18] observed an increase of *Lactobacillus* genus by 7 times after 11 wk of supplementation of *L. fermentum*, which may suggest an effect of probiotics in gut microbiota composition [18]. Martarelli et al. [26] have also supplemented athletes with *Lactobacillus* species and, at the end of the study, found a significant augment of *Lactobacillus* count in feces. Lactic acid bacteria produce lactate that is converted by butyrate-producing bacteria into butyric acid. This short chain fatty acid (SCFA) is pivotal for intestinal homeostasis because of its several benefits in the intestinal cells—mainly barrier function and permeability because the butyrate up-regulate tight junction proteins [27]. In addition, it seems that symbiotic supplementation may have an additional effect on GI symptoms and gut permeability, as reported by Roberts [25]. On the other hand, West et al. [28] in a study with non-athletes did not identify differences between symbiotic and prebiotic groups regarding SCFA production or gut permeability [28]. Still, the effect of probiotics, prebiotics, and symbiotics on SCFA production and gut permeability in athletes is still not elucidated.

Recovery and strength exercise

Recently studies have targeted the possible link between probiotics use in muscle repair [29,30]. Although these authors propose that probiotics may speed up muscle repair, their evidence involves resistance training in addition to other nutritional supplements that have a direct influence on protein synthesis (e.g., whey protein, β -hydroxy- β -methylbutyrate). Furthermore, the main purpose of these studies was the possible increase in proteins'

absorptive capacity with probiotic [29,30] or recovery process, whereas immune cell parameters was not evaluated. Indirectly probiotics may lower muscle repair process time [29].

In addition, in strength sports, probiotics may contribute to muscle hypertrophy processes [29] or be associated with the regulation of intestinal health. Strength athletes normally have a high consumption of proteins, which can lead to an increase in the production of hydrogen sulphate. This later may be detrimental to intestinal health [29]. Preserving athletes' health indirectly aids sports performance. Hence it seems that probiotics may have clinical contributions through different ways in sports modalities.

Proposed mechanisms of probiotics action

The main ways that probiotics may act are enhancing the barrier function, stimulating immune cells activity (regulating the pro-/antiinflammatory pathways and immunoglobulins production), increasing SCFA production, lowering intestinal pH, and stimulating mucus production [1,2].

In a sports context, studies suggest possible mechanisms by which probiotics may improve the immune function of athletes related to increased IFN- γ production by T lymphocytes [16,17] and a possible link to increased IgA production by B lymphocytes [17]. According to Glück and Gebbers [31], immune cells can traffic from one mucosal site to another in the body and the stimulation at one site (e.g., intestine) can result in effects detectable at another site (e.g., respiratory tract).

Regarding gut permeability, the authors suggest that toll-like receptor 2 (TLR2) activation may culminate in tight junction protein production, especially zonulin, which occurs with the probiotic use [21]. As reported by Cario et al. [32] and Wells et al. [33], this occurs via TLR2 present in the gut cell surface, which activates the inflammatory cascade, stimulating nuclear factor κ B transcription factor and MyD88, which in a tonic level activation preserve epithelial intestinal integrity (Fig. 1). Commensal bacterial stimulation of TLR2 in the intestinal epithelium may be necessary for intestinal homeostasis and to prevent endotoxemia [25].

Which factors may influence probiotics outcomes?

It seems that there is a minimum time necessary for probiotic use to induce the positive effects expected in the immune system of athletes. In a study by Gill et al. [10] with short-term high-dose probiotic use (*L. casei* 1×10^{11} per seventh days), the probiotic group did not have alterations in systemic cytokine profile or gut permeability compared with placebo [10]. The majority of studies that reported positive effects employed long periods of probiotics administration [7,14,15,18–22,25].

Some authors [11,17,24] have reported that probiotic consumption for 4 wk led to positive effects related to URS and GI symptoms. Both the Haywood and Shing studies [11,24] employed a multispecies probiotic with increased load and dose per strain. Perhaps this explains their results. Multispecies supplements with different characteristics have an enhanced colonization chance and display synergistic effects with specific properties to enhance the chance of survival and adhesion. Moreover, the positive interrelationships among strains may increase their biological activity. Colonization of probiotics species is probably host dependent because of gastrointestinal complexity and variability [34].

Cox et al. [17] reported a reduction in number of days with illness symptoms and a modest increase in IgA salivary concentration after employing a monostrain (*L. fermentum* VRI-003 [PCC]; 12×10^9 CFU/d). As reported by authors, this specific probiotic strain has a potential to colonize the intestinal tract, and this may justify the described result.

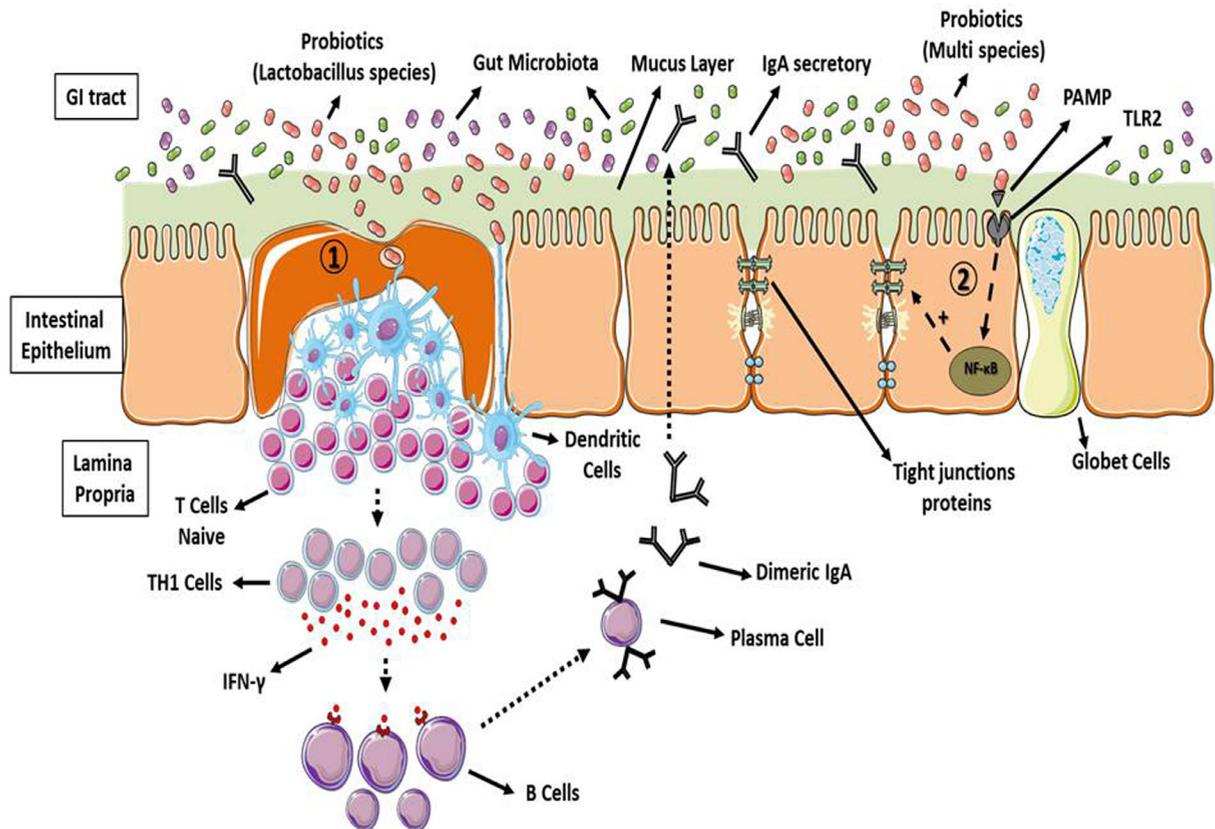


Fig. 1. Probiotics effects on gut barrier. (1) *Lactobacillus* species may have a role on IgA secretory production via IFN- γ -producing Th1 cells pathway [16,17]. These species influence the mucosal immune system by interacting with intestinal epithelial cells, M cells, and dendritic cells. The GI mucosa interconnects with upper respiratory tracts, which may explain the improvement in GI symptoms and severity of URS [7]. (2) Specific probiotics stimulate TLR2 signaling through its molecular patterns (PAMPs), leading to an inflammatory response (NF- κ B pathway). The inflammatory mediators may cause positive adaptations in the intestinal barrier to control this response. GI, gastrointestinal; IFN- γ , interferon γ ; NF- κ B, nuclear factor κ B; PAMP, pathogen-associated molecular pattern; Th1, T helper 1 cells; TJP, tight junction proteins; TLR2, Toll-like receptor 2; URS, upper respiratory illness symptoms.

Conclusions and future perspectives

Specific probiotics (or multispecies) appear to be effective in minimizing GI symptoms and URS and perhaps postexercise recovery. These effects are dependent on the species, dose, and period and form of administration (e.g., capsules, sachets, fermented milk). The cellular mechanisms related to the effectiveness of probiotics in the sports context have not yet been elucidated, and few articles have reported biological assessments. The possible mechanisms of action of probiotics have already been described in studies outside of sports. It is suggested that future research consider parameters such as SCFA production, pH changes, barrier function-related proteins, microbiota composition, and immunologic cells function modulated by exercise intensity and duration.

Acknowledgments

The authors of University of São Paulo wish to thank Professor Nicholas West for his relevant contributions.

References

- [1] Pyne DB, West NP, Cox AJ, Cripps AW. Probiotics supplementation for athletes: clinical and physiological effects. *Eur J Sport Sci* 2015;15:63–72.
- [2] Berman S, Petriz B, Kajėnienė A, Prestes J, Castell L, Franco OL. The microbiota: an exercise immunology perspective. *Exerc Immunol Rev* 2015;21:70–9.
- [3] Clark A, Mach N. Exercise-induced stress behavior, gut-microbiota-brain axis and diet: a systematic review for athletes. *J Int Soc Sports Nutr* 2016;24:43.
- [4] Maughan RJ, Burke LM, Dvorak J, Larson-Meyer DE, Peeling P, Phillips SM, et al. IOC Consensus Statement: dietary supplements and the high-performance athlete. *Int J Sport Nutr Exerc Metab* 2018;28:104–25.
- [5] Gill SK, Teixeira A, Rama L, Prestes J, Rosado F, Hankey J, et al. Circulatory endotoxin concentration and cytokine profile in response to exertional-heat stress during a multi-stage ultra-marathon competition. *Exerc Immunol Rev* 2015;21:114–28.
- [6] Pugh JN, Fearn R, Morton JP, Close GL. Gastrointestinal symptoms in elite athletes: Time to recognise the problem? *Br J Sports Med* 2018 Apr;52:487–8.
- [7] Gleeson M, Bishop NC, Oliveira M, Tauler P. Daily probiotic's (*Lactobacillus casei* Shirota) reduction of infection incidence in athletes. *Int J Sport Nutr Exerc Metab* 2011;21:55–64.
- [8] West NP, Pyne DB, Peake JM, Cripps AW. Probiotics, immunity and exercise: a review. *Exerc Immunol Rev* 2009;15:107–26.
- [9] Colbey C, Cox AJ, Pyne DB, Zhang P, Cripps AW, West NP. Upper respiratory symptoms, gut health and mucosal immunity in athletes. *Sports Med* 2018;48 (Suppl 1):65–77.
- [10] Gill SK, Allerton DM, Ansley-Robson P, Hemmings K, Cox M, Costa RJ. Does short-term high dose probiotic supplementation containing *Lactobacillus casei* attenuate exertional-heat stress induced endotoxaemia and cytokinaemia? *Int J Sport Nutr Exerc Metab* 2016;26:268–75.
- [11] Haywood BA, Black KE, Baker D, McGarvey J, Healey P, Brown RC. Probiotic supplementation reduces the duration and incidence of infections but not severity in elite rugby union players. *J Sci Med Sport* 2014;17:56–60.
- [12] Gleeson M. Immune function in sport and exercise. *J Appl Physiol* 2007;103:693–9.
- [13] Walsh NP, Gleeson M, Shephard RJ, Gleeson M, Woods JA, Bishop NC, et al. Position statement. Part one: immune function and exercise. *Exerc Immunol Rev* 2011;17:6–63.
- [14] Gleeson M, Bishop NC, Struszczyk L. Effects of *Lactobacillus casei* Shirota ingestion on common cold infection and herpes virus antibodies in endurance athletes: a placebo-controlled, randomized trial. *Eur J Appl Physiol* 2016;116:1555–63.
- [15] Strasser B, Geiger D, Schauer M, Gostner JM, Gatterer H, Burtscher M, et al. Probiotic supplements beneficially affect tryptophan-kyurenine metabolism and

- reduce the incidence of upper respiratory tract infections in trained athletes: a randomized, double-blinded, placebo-controlled trial. *Nutrients* 2016;8. pii: E752.
- [16] Clancy RL, Gleeson M, Cox A, Callister R, Dorrington M, D'Este C, et al. Reversal in fatigued athletes of a defect in interferon gamma secretion after administration of *Lactobacillus acidophilus*. *Br J Sports Med* 2006;40:351–4.
- [17] Cox AJ, Pyne DB, Saunders PU, Fricker PA. Oral administration of the probiotic *Lactobacillus fermentum* VRI-003 and mucosal immunity in endurance athletes. *Br J Sports Med* 2010;44:222–6.
- [18] West NP, Pyne DB, Cripps AW, Hopkins WG, Eskesen DC, Jairath A, et al. *Lactobacillus fermentum* (PCC[®]) supplementation and gastrointestinal and respiratory-tract illness symptoms: A randomized control trial in athletes. *Nutr J* 2011;10:30.
- [19] Kekkonen RA, Vasankari TJ, Vuorimaa T, Haahtela T, Julkunen I, Korpela R. The effect of probiotics on respiratory infections and gastrointestinal symptoms during training in marathon runners. *Int J Sport Nutr Exerc Metab* 2007;17(3):52–63.
- [20] West NP, Horn PL, Pyne DB, Gebiski VJ, Lahtinen SJ, Fricker PA, et al. Probiotic supplementation for respiratory and gastrointestinal illness symptoms in healthy physically active individuals. *Clin Nutr* 2014;33:581–7.
- [21] Lamprecht M, Frauwallner A. Exercise, intestinal barrier dysfunction and probiotic supplementation. *Med Sport Sci* 2012;59:47–56.
- [22] Michalickova D, Minic R, Dikic N, Andjelkovic M, Kostic-Vucicevic M, Stojmenovic T, et al. *Lactobacillus helveticus* Lafti L10 supplementation reduces respiratory infection duration in a cohort of elite athletes: a randomized, double-blind, placebo-controlled trial. *Appl Physiol Nutr Metab* 2016;41:782–9.
- [23] Jeukendrup AE, Vet-Joop K, Sturk A, Stegen JH, Senden J, Saris WH, et al. Relationship between gastrointestinal complaints and endotoxaemia, cytokine release and the acute phase reaction during and after a long-distance triathlon in highly trained men. *Clin Sci (Lond)* 2000;98:47–55.
- [24] Shing CM, Peake JM, Lim CL, Briskey D, Walsh NP, Fortes MB, et al. Effects of probiotics supplementation on gastrointestinal permeability, inflammation and exercise performance in the heat. *Eur J Appl Physiol* 2014;114:93–103.
- [25] Roberts JD, Suckling CA, Peedle GY, Murphy JA, Dawkins TG, Roberts MG. An exploratory investigation of endotoxin levels in novice long distance triathletes, and the effects of a multi-strain probiotic/prebiotic, antioxidant intervention. *Nutrients* 2016;8. pii: E733.
- [26] Martarelli D, Verdenelli MC, Scuri S, Cocchioni M, Silvi S, Cecchini C, et al. Effect of a probiotic intake on oxidant and antioxidant parameters in plasma of athletes during intense exercise training. *Curr Microbiol* 2011;62:1689–96.
- [27] Chun C, Zheng L, Colgan SP. Tissue metabolism and host-microbial interactions in the intestinal mucosa. *Free Radic Biol Med* 2017;105:86–92.
- [28] West NP, Pyne DB, Cripps AW, Christophersen CT, Conlon MA, Fricker PA. Gut Balance, a symbiotic supplement, increases fecal *Lactobacillus paracasei* but has little effect on immunity in healthy physically active individuals. *Gut Microbes* 2012;3:221–7.
- [29] Jäger R, Shields KA, Lowery RP, de Souza EO, Partl JM, Hollmer C, et al. Probiotic *Bacillus coagulans* GBI-30, 6086 reduces exercise-induced muscle damage and increases recovery. *Peer J* 2016;4:e2276.
- [30] Gepner Y, Hoffman JR, Shemesh E, Stout JR, Church DD, Varanoske AN, et al. Combined effect of *Bacillus coagulans* GBI-30, 6086 and HMB supplementation on muscle integrity and cytokine response during intense military training. *J Appl Physiol* (1985) 2017;123:11–8.
- [31] Glück U, Gebbers JO. Ingested probiotics reduce nasal colonization with pathogenic bacteria. *Am J Clin Nutr* 2003;77:517–20.
- [32] Cario E, Gerken G, Podolsky DK. Toll-like receptor 2 controls mucosal inflammation by regulating epithelial barrier function. *Gastroenterology* 2007;132:1359–74.
- [33] Wells JM, Rossi O, Meijerink M, van Baarlen P. Epithelial crosstalk at the microbiota-mucosal interface. *Proc Natl Acad Sci U S A* 2011;108(Suppl 1):4607–14.
- [34] Timmerman HM, Koning CJ, Mulder L, Rombouts FM, Beynen AC. Monostrain, multistrain and multispecies probiotics—a comparison of functionality and efficacy. *Int J Food Microbiol* 2004;96:219–33.
- [35] Gleeson M, Bishop NC, Oliveira M, McCauley T, Tauler P, Lawrence C. Effects of a *Lactobacillus salivarius* probiotic intervention on infection, cold symptom duration and severity, and mucosal immunity in endurance athletes. *Int J Sport Nutr Exerc Metab* 2012;22:235–42.