

The effects of combined probiotic ingestion and circuit training on muscular strength and power and cytokine responses in young males

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Abstract: To our knowledge, the efficacy of combined probiotic supplementation with circuit training has not been evaluated. Thus, we investigated the effects of probiotic supplementation combined with circuit training on isokinetic muscular strength and power and cytokine responses in young males. Forty-eight healthy sedentary young males were recruited and randomised into 4 separate groups: sedentary placebo control, probiotics (P), circuit training with placebo (CT), and circuit training with probiotics (CTP). Participants in the CT and CTP groups performed circuit training 3 times/week with 2 circuits of exercises from weeks 1–8 followed by 3 circuits of exercises from weeks 9–12. Participants in the P and CTP groups consumed multi-strain probiotics containing 3×10^{10} colony-forming units of *Lactobacillus acidophilus*, *L. lactis*, *L. casei*, *Bifidobacterium longum*, *B. bifidum* and *B. infantis* twice daily for 12 weeks. Measurements of body height and weight, blood pressure, resting heart rate, blood samples, and isokinetic muscular strength and power were carried out at pre- and post-tests. Isokinetic knee strength and power in CT and CTP groups were significantly higher ($P < 0.05$) at post-test. In addition, interleukin (IL)-10 concentration was significantly increased ($P < 0.0001$) at post-test in P and CT but a trend toward significant increase in CTP ($P = 0.09$). Nevertheless, there was no significant difference in IL-6. This study suggests that 12 weeks of circuit training alone and the combination of circuit training and probiotic consumption improved muscular performance while circuit training alone and probiotics alone increased IL-10 concentration.

Key words: supplement, exercise, isokinetic, IL-6, IL-10.

Résumé : L'efficacité de la supplémentation en probiotiques combinée à l'entraînement en circuit n'a pas fait, à notre connaissance, l'objet d'une évaluation. Le but de cette étude est donc d'examiner les effets de la supplémentation en probiotiques combinée à l'entraînement en circuit, et ce, sur la force et la puissance des muscles et la réponse des cytokines chez de jeunes hommes. On recrute 48 jeunes hommes en bonne santé et sédentaires et on les répartit de façon aléatoire dans 4 groupes distincts : contrôle, sédentaire et placebo, probiotiques (« P »), entraînement en circuit avec placebo (« CT ») et entraînement en circuit avec probiotiques (« CTP »). Les sujets des groupes CT et CTP participent, à raison de 3 x/semaine, à l'entraînement en circuit comprenant 2 circuits d'exercice durant les semaines 1–8 et 3 circuits durant les semaines 9–12. Les sujets des groupes P et CTP consomment durant 12 semaines, à raison de 2 x par jour, des probiotiques de souches multiples comprenant 3×10^{10} cellule souche unipotente de *Lactobacillus acidophilus*, *L. lactis*, *L. casei*, *Bifidobacterium longum*, *B. bifidum* et *B. infantis*. Avant et après les tests, on évalue la stature, la masse corporelle, la pression sanguine, la fréquence cardiaque de repos; on prélève des échantillons de sang et on mesure la force et la puissance des muscles en contraction isokinétique. Au post-test, les groupes CT et CTP présentent des valeurs significativement plus élevées de force et de puissance des extenseurs du genou en contraction isokinétique ($P < 0,05$). Au post-test aussi, les groupes P et CT présentent des concentrations d'interleukines (« IL »)-10 significativement plus élevées ($P < 0,0001$) et le groupe CTP présente seulement une tendance à l'augmentation ($P = 0,09$). Toutefois, on ne note pas de différence significative des IL-6. D'après ces résultats, 12 semaines d'entraînement en circuit seul et la combinaison de l'entraînement en circuit et de la consommation de probiotiques améliorent la performance musculaire alors que l'entraînement en circuit seul et la consommation de probiotiques seule suscitent une augmentation de la concentration des IL-10. [Traduit par la Rédaction]

Mots-clés : supplément, exercice physique, isokinétique, IL-6, IL-10.

Introduction

The role of commensal microbiota in bolstering our health has been extensively carried out by many researchers (Daliri and Lee 2015; de Almada et al. 2015). Probiotics are defined by the World Health Organization as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host” (Food and Agriculture Organization (FAO) 2002). These nonpatho-

genic microorganisms can be found in fermented food products such as yoghurt, kefir, tempeh, cabbage kimchee, sauerkraut, natto, soybean-based miso, and probiotic drink.

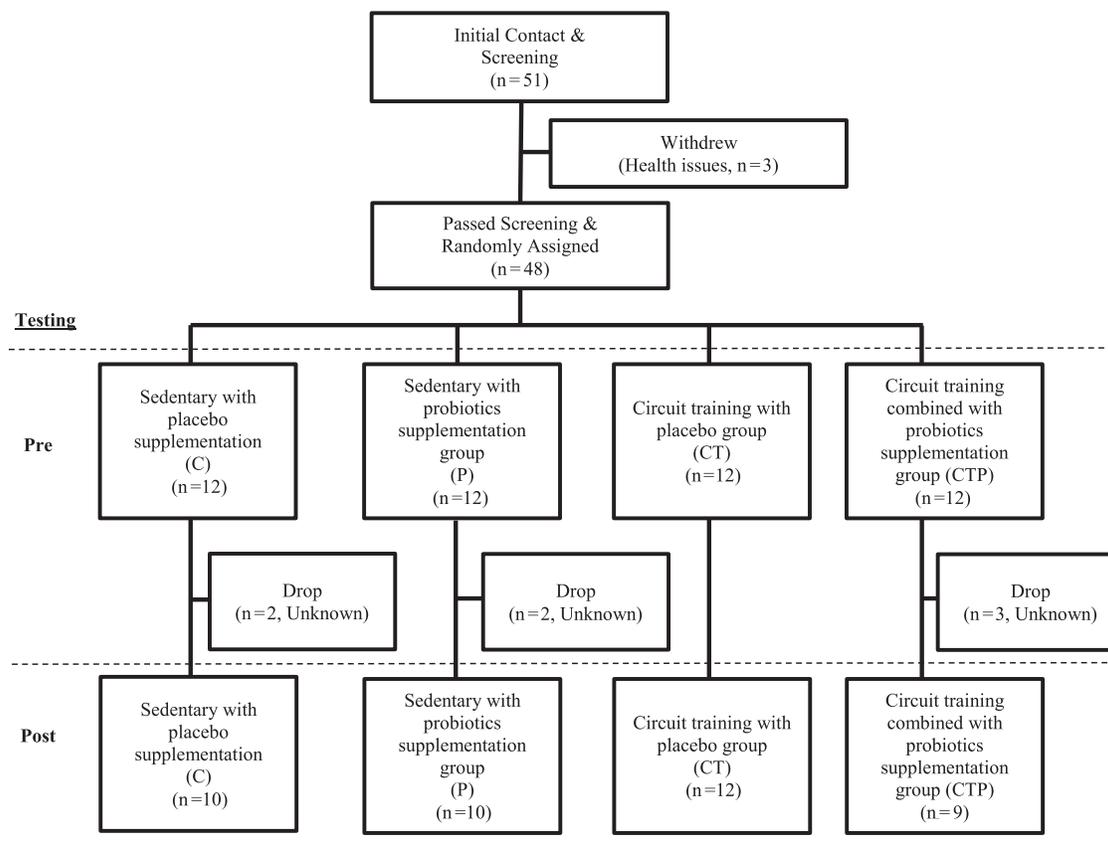
The diversity of microbiota composition, whether in a multi-strain probiotic or in a single-strain probiotic, has been proposed as a supplement as it can modulate the anti-inflammatory (i.e., interleukin (IL)-10) and pro- (i.e., IL-6) cytokines in the body to promote a better health over the course of training (Jäger et al.

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Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) diagram of study recruitment, enrollment, randomisation, and analysis.

2016; Pedersen et al. 2001). The mechanisms of probiotics that actually help to regulate inflammation include (i) indirect effects by boosting the production of short-chain fatty acids with anti-inflammatory properties (Vinolo et al. 2011), increasing the synthesis of antimicrobial peptides that influence inflammation resolution pathways in the mucosa (Schlee et al. 2008), as well as protecting or repairing epithelial barriers (Bermudez-Brito et al. 2012; Thomas and Versalovic 2010); and (ii) direct effects by binding with the innate immune receptors (Thomas and Versalovic 2010) and triggering pathways that will cause the production of cytokines related to the inflammation (Jeon et al. 2012). Nevertheless, despite this attention to probiotics, studies done to investigate the effects of probiotics and exercise training are scarce, especially on muscular performance.

Circuit training that involves resistance exercise has been shown to improve muscular strength and power (Chen et al. 2014; Lau and Ooi 2014). However, besides muscular improvement, muscular damage may also occur especially among the sedentary population when they participate in resistance training (Chevion et al. 2003; Roth et al. 2000). The inflammation that occurs in the muscle is one of the important mechanisms for muscular adaptation towards exercise so that the muscle can regenerate and repair itself (Peake et al. 2017). Longer period to recover may interrupt daily activities and lead to a longer break from physical exercise. Nevertheless, the consumption of probiotics was believed to play a role with nutrients in the intestines (Sheridan et al. 2014), leading to beneficial effect in faster muscle recovery rate (Jäger et al. 2015).

To date, evidence of the combined effects of resistance exercise and probiotic supplementation on interleukins and muscular performance is still lacking. Therefore, the present study was proposed to investigate the combined effects of probiotic supplementation with circuit training on muscular strength and power and

cytokine responses in young males following 12 weeks of the intervention period.

Materials and methods

Participants

In this study, 48 participants were recruited via snowball sampling among Universiti Sains Malaysia students after considering possibilities of drop-out. The inclusion criteria included (i) healthy young males with a sedentary lifestyle (not engaged in any physical training programme and exercise no more than twice per week), (ii) aged between 19 to 26 years old, and (iii) not consuming any nutritional supplements or ergogenic aids prior to the study. The exclusion criteria include (i) smoking/vaping, (ii) on medication, and (iii) having chronic diseases.

Research procedures

A randomised, parallel, placebo-controlled study design was employed. The procedure for this study has been approved by the Human Research Ethics Committee, Universiti Sains Malaysia, Kelantan (JEPeM Code: USM/JEPeM/15040132) and was in accordance with the Declaration of Helsinki as revised in 1983. The participants signed an informed consent form prior to participating in the study. Measurements were conducted at pre- and post-test of the 12-week intervention period. The measurements included body height (SECA, UK) and weight (TANITA TBF-410, Japan), blood pressure and resting heart rate (OMRON, Japan), 4 mL of blood samples, and isokinetic muscular strength and power test (Biodex System 3 Pro, New York, N.Y., USA).

Then, the participants were randomly assigned into the following 4 groups based on their age and body mass index (BMI) (see Fig. 1): 12 weeks of sedentary with placebo supplementation group (C), sedentary with probiotic supplementation group (P), circuit

Table 1. Physiological characteristics of the participants.

Variable	Testing period	Age (y)	Body height (cm)	Body weight (kg)	BMI (kg/m ²)	Body fat percentage (%)	Resting HR (bpm)	SBP (mm Hg)	DBP (mm Hg)
C (n = 10)	Pre-test	22±2	170.4±7.2	61.4±10.4	21.1±2.8	18.6±7.3	72.9±2.6	117.6±3.7	70.4±1.1
	Post-test			61.8±10.5	21.3±2.9	19.8±7.2	72.6±3.4	120.0±2.7	71.8±1.5
P (n = 10)	Pre-test	23±1	169.8±5.0	63.0±10.3	21.8±3.4	20.5±6.4	72.2±3.5	120.7±3.4	68.6±2.4
	Post-test			62.4±11.5	21.5±3.8	20.1±6.7	68.5±2.3	121.4±3.0	71.0±2.2
CT (n = 12)	Pre-test	21±2	169.3±7.0	60.6±9.9	21.1±2.7	18.3±6.8	71.7±2.5	118.0±3.2	70.7±1.5
	Post-test			60.9±10.0	21.2±2.8	19.3±6.7	71.2±3.5	120.0±2.4	69.1±3.1
CTP (n = 9)	Pre-test	22±3	170.2±5.1	64.1±10.2	22.1±3.4	21.1±6.4	72.4±3.1	121.0±3.8	71.4±2.4
	Post-test			63.7±11.4	21.9±3.9	20.7±6.8	68.3±2.6	121.8±3.3	71.1±3.5

Note: Values are tabulated as means ± SD. BMI, body mass index; C, sedentary with placebo control group; CT, exercise group; CTP, combined probiotics with exercise group; DBP, diastolic blood pressure; HR, heart rate; P, probiotics group; SBP, systolic blood pressure.

training with placebo group (CT), and 12 weeks of circuit training combined with probiotic supplementation group (CTP). A checklist to record participant's weekly activity and adherence to the supplementation regimen was given to the participants.

Post-test measurements, which were similar to the pre-test measurements, were carried out following the 12-week intervention period. Subsequently, blood serum for IL-6 and IL-10 were analysed based on enzyme-linked immune sorbent assay (ELISA) method by using a reagent kit (Human IL-6 and IL-10 ELISA Kit, China).

Probiotic and placebo supplementation

The probiotic and placebo used in this study were prepared by B Crobes Laboratory Sdn. Bhd., which was registered with the Malaysian Ministry of Health (121/14) and was certified Halal (A15766). The participants consumed 2 sachets of probiotic per day (P and CTP) or placebo (C and CT) for 12 weeks. Probiotic (microbial cell preparation) used in this study was known as Hexio granule and it contains 6 different microorganism strains (*Lactophilus acidophilus* BCMC 12130, *L. casei* BCMC 12313, *L. lactis* BCMC 12451, *Bifidobacterium bifidum* BCMC 02290, *B. infantis* BCMC 02129, and *B. longum* BCMC 02120) in each sachet with a concentration of 3×10^{10} colony-forming units during the manufacturing. It is an orange-flavoured and cream-coloured granular powder. The nutritional compositions in each of the probiotics sachet are carbohydrate (2.0 g), lactose (1.28 g), sugar (0.12 g), protein (0.16 g), fat (0.01 g), and fibre (0.01 g), and an energy value of 11.55 kcal. As for placebo, it was identical in shape, taste, and colour to the probiotics but contained no bacteria.

Circuit-training programme

Participants in the CT and CTP groups performed circuit training 3 times per week with 2 circuits of exercises from weeks 1–8 followed by 3 circuits of exercises from weeks 9–12. Each circuit comprised 10 stations (1 type of exercise per station) with work to rest ratio of 1:2 and the resting period between circuits were 5 min. The exercises included heel raise with dumbbell, side lateral raise with elastic band, leg abduction with elastic band, shoulder extension and flexion using elastic band, rope skipping, triceps extension with dumbbell, half squat with elastic band, standing chest fly with dumbbell, leg curl with elastic band, as well as biceps curl with dumbbell. The weight of the dumbbell and elasticity of the elastic band used was progressively increased by 1–2.5 kg, depending on individuals' capacity after 5 weeks of intervention, and remained the same until the end of the 12 weeks of intervention. The prescribed exercise regimen used in this study has been used in several previous studies (Chen et al. 2016; Lau and Ooi 2014; Ooi et al. 2015).

Isokinetic muscular strength and power measurement

The muscular performance of the participants was measured during pre- and post-tests by measuring their muscular strength (peak torque) and power via an isokinetic dynamometer (Biodex System 3 Pro). The 2 angular velocities used to measure flexion

and extension of the knee were $90^\circ \cdot s^{-1}$ and $300^\circ \cdot s^{-1}$. These angular velocities were chosen based on other similar studies (Chen et al. 2016; Ooi et al. 2015).

To begin the test, the participant was seated while leaning against a backrest that was tilted 85° from the horizontal plane. The participant's shoulder, waist, and thigh were strapped to minimise body movement and to ensure stabilisation of the body during the test. The lateral femoral epicondyle was used as the body landmark for matching the axis of rotation of the dynamometer resistance adaptor. Once the participant was seated in a position that allowed for a comfortable and unrestricted motion for the knee extension and flexion (from a position of 90° of flexion to terminal extension), the following measurements were taken: seat height, seat inclination, dynamometer head height, and resistance pad level. These measurements were recorded and stored on the Biodex Advance Software program in an attempt to identify and reproduce similar testing positions for each individual participant. Gravity correction was obtained by measuring the torque exerted on the dynamometer resistance adaptor with the knee in the relaxed state at the terminal extension.

Before the testing began, the procedure was fully informed to the participants. They were asked to do 5 repetitions for the $90^\circ \cdot s^{-1}$ angular velocity and 10 repetitions for the $300^\circ \cdot s^{-1}$ angular velocity. The participant was given 60 s to rest between the 2 angular velocities. The testing was repeated on the other side of the limb. All testing procedures as well as verbal encouragement were given by the same investigator for all participants.

Statistical analysis

Statistical analysis was performed by using IBM SPSS (version 22.0; IBM Corp., Armonk, N.Y., USA). Mixed-factorial ANOVA was performed to determine the significance of differences between and within groups. Differences considered significant at $P < 0.05$. Results were reported as the means ± SD.

Results

Physiological characteristics of the participants

Forty-eight participants were recruited at the beginning of the study with 12 participants per group. However, 7 participants dropped out during the intervention because of personal reasons and did not complete post-test measurements. The mean age, body height, body weight, BMI, body fat percentage, mean resting heart rate, and systolic and diastolic blood pressure of the participants according to the group are shown in Table 1.

Adherence to the training and supplementation regimen

There was a total of 36 training days during the 12-week intervention. The adherence rate of the participants to the exercise training was more than 90%. A total of 168 sachets (either placebo or probiotics) was consumed by each participant during the 3-month intervention period and the adherence to the supplementation regimen was more than 95%.

Probiotics/placebo combined with exercise training increased muscular strength and power

Results for the muscular strength and power are presented in Fig. 2. There were no significant differences in all the measured parameters between all the groups. However, isokinetic knee strength and power in the CT and CTP groups were significantly higher in dominant knee peak torque at $90^{\circ}\cdot\text{s}^{-1}$ ($P = 0.005$), dominant knee extension average power at $300^{\circ}\cdot\text{s}^{-1}$ ($P = 0.002$), dominant knee flexion average power at $300^{\circ}\cdot\text{s}^{-1}$ ($P = 0.042$), nondominant knee extension peak torque at $90^{\circ}\cdot\text{s}^{-1}$ ($P = 0.034$), nondominant knee flexion peak torque at $90^{\circ}\cdot\text{s}^{-1}$ ($P = 0.004$), nondominant knee extension average power at $300^{\circ}\cdot\text{s}^{-1}$ ($P = 0.038$), and nondominant knee flexion average power at $300^{\circ}\cdot\text{s}^{-1}$ ($P = 0.002$) at post-test when compared with respective pre-test values.

Probiotics alone and exercise alone increased serum IL-10 concentration

There were no significant differences in all the measured parameters between all the groups (Table 2). Nevertheless, further analysis showed that there was a significant difference ($P = 0.001$) in mean serum IL-10 concentration at post-test compared with pre-test in P and CT groups.

Probiotics/placebo with or without exercise had no effect on serum IL-6 concentration

There were no significant differences in all the measured parameters between all the groups (see Table 2). Further analysis also showed that there was also no significant difference of mean serum IL-6 concentration within each group based on time ($P = 1.00$).

Discussion

Our results indicated that there were no significant differences between the C, CT, P, and CTP groups on the muscular strength and power measured in the present study. However, significant increases were observed after the 12-week intervention period in the CT and CTP groups. It is well accepted that resistance exercise induces muscular strength and power (Alcaraz et al. 2011; Arazi and Asadi 2012; Chtara et al. 2008). The increment in muscular strength and power during the first few weeks of resistance training has been attributed to the neural adaptations (Moritani and deVries 1979). These adaptations provide more efficient neural pathways along the route to the muscles. The consequence is an increased activation of synergistic muscles, along with the inhibition of neural protective mechanisms (Folland and Williams 2007), and thus induces the muscle's ability to generate more force. In the present study, participants in both the CT and CTP groups followed the exercise-training programme for 12 weeks. Thus, the observed increase in muscular strength and power in these 2 groups could also be attributed to the hypertrophy of the muscle fibres (Sale 1988).

The combined effect of probiotic and exercise that lead to improvement in muscular strength and power was also reported in the previous study (Georges et al. 2014; Jäger et al. 2016). Even though the mechanism of the probiotics and its relation to the muscular strength is unclear, the significant increment obtained in the present study may be attributed to the probiotics mechanism that may have the tendency to increase the protein absorption in the body.

In addition, our data also indicated that there was an increasing trend in muscular strength and power among the participants in the P group despite the absence of statistical significance in the present study. This shows that the probiotic consumption alone may potentially improve the muscular strength. Despite negligible findings in the literature to support this trend, the consumption of probiotics may be associated with the energy enhancement that helped produce more strength in the muscles. In the body, especially in the human gut, there is a process known as carbohydrate fermentation, which is the core activity of the human gut

microbiota that causes the production of energy and carbon metabolism of the colon (Lamprecht and Frauwallner 2012). Moreover, the interaction of the microorganism in the gastrointestinal lining with the range of end products generated by protein digestion, for example, amino acids, is also believed to enhance energy production in the body (Kimmel et al. 2010; Lamprecht and Frauwallner 2012) and hence may have resulted in the increment trend in muscular strength observed in the current study.

Furthermore, the finding of a significant increase in IL-10 concentration in the CT group was similar to a study done by Calle and Fernandez (2010). Muscle contractions induced by exercise training employed in this study may have caused muscular damage (Calle and Fernandez 2010). Therefore, increased IL-10 production could be a concomitant inflammatory response. In addition, it was also speculated that resistance exercise might affect the magnitude of metabolic demand or fatigue, which may further influence the increment in the cytokine response patterns (Izquierdo et al. 2009), thus perhaps explaining the increasing concentration of IL-10 in the present study.

Similar significant increment was also observed in the P group after the 12-weeks intervention. This finding is consistent with the other studies that also found an increment in the IL-10 concentration after consuming probiotics (Čitar et al. 2014; Sheil et al. 2006). Despite muscular damage and fatigue as observed in CT group, the increment of IL-10 concentration in the P group could have played an important role in ameliorating the symptoms of inflammatory bowel diseases. Some of the participants in the P group did mention that they were having diarrhoea and this problem was eventually solved after taking the probiotic supplement. Hence, this provides a rationale use of probiotic supplement for the treatment of gastrointestinal inflammation as it already had been proven in other studies (Goldenberg et al. 2015; Guandalini 2011). For that reason, it is important to monitor the symptoms of inflammatory bowel diseases for future studies. The trend of IL-10 concentration in the CTP group also increased after 12 weeks of intervention. To our knowledge, there is no other study to support this result at the moment as research in this area is very scarce. Nevertheless, this might be due to the reduction in muscle damage that speeds up recovery rate. Probiotics have been reported to lessen the severity, number, and duration of infections in athletes (Cox et al. 2010; Gleeson et al. 2011; Haywood et al. 2014). Hence, the probiotic consumption was believed to interact with nutrients absorption (Sheridan et al. 2014), leading to beneficial faster muscle recovery rate (Jäger et al. 2015). The probiotics increase the gut lining cells health by enhancing the nutrient absorption including minerals, peptides, and amino acids by lowering the inflammation rate and supporting optimum development of the absorptive area of the villi (Kimmel et al. 2010).

No significant difference was observed in IL-6 after the intervention period. Nevertheless, its increasing trend was observed at post-test measurement. The increasing trend in IL-6 concentration in the present study was consistent with a study done by Cullen et al. (2016). It has been reported that contracting muscles contribute to most of the IL-6 present in the circulation in response to exercise, where the magnitude of the exercise-induced IL-6 response is dependent on the intensity and especially duration of the exercise while the mode of exercise has little effect. However, a prolonged exercise involving a significant muscle mass in the contractile activity is necessary to produce a marked systemic IL-6 response. Thus, our prescribed circuit training program may not have reached the required intensity and duration to elicit the significant increase in IL-6. Shing et al. (2014) also reported that probiotic supplementation caused increased in plasma concentrations of IL-6 and IL-10. Smaller perturbation was also observed in IL-6 and IL-10 concentrations after 11 weeks of probiotic supplementation in male and female competitive cyclists (West et al. 2011).

Fig. 2. Mean dominant (a) and nondominant (b) knee-extension peak torque at $90^{\circ}\cdot s^{-1}$, mean dominant (c) and nondominant (d) knee-flexion peak torque at $90^{\circ}\cdot s^{-1}$, mean dominant (e) and nondominant (f) knee-extension average power at $300^{\circ}\cdot s^{-1}$, and mean dominant (g) and nondominant (h) knee-flexion average power at $300^{\circ}\cdot s^{-1}$. *, Significant difference from pre-test ($P < 0.05$).

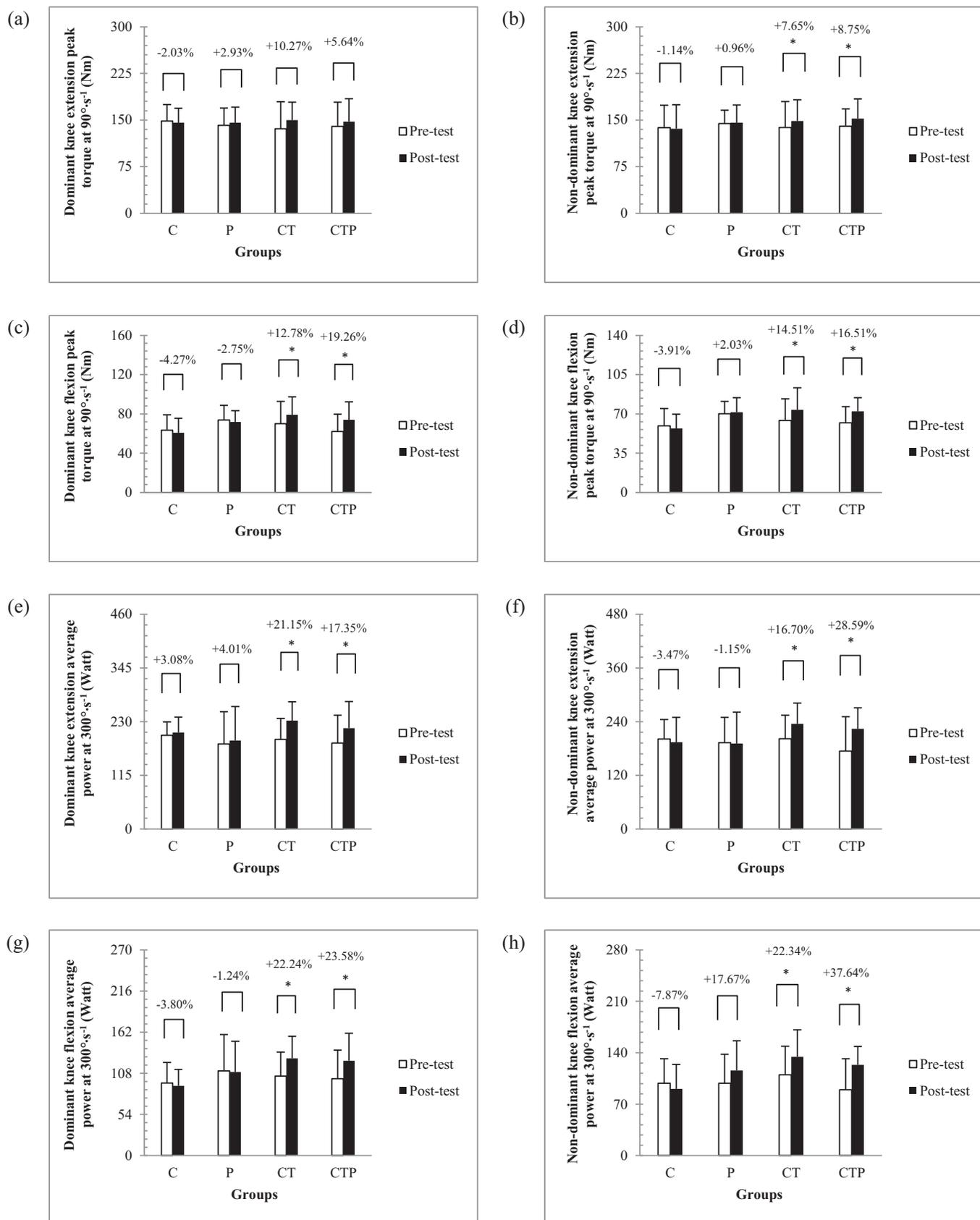


Table 2. IL-6 and IL-10 concentrations before and after the intervention.

Groups	IL-6 concentration (pg/mL)			IL-10 concentration (pg/mL)		
	Pre-test	Post-test	Percent difference (%)	Pre-test	Post-test	Percent difference (%)
C	13.99±1.06	14.36±2.07	+2.64	4.82±1.99	7.21±0.83	+49.59
P	13.12±1.61	12.66±1.50	-3.51	5.99±1.29	9.99±4.93*	+66.78
CT	12.83±1.57	13.77±1.01	+7.33	5.20±1.71	9.23±2.96*	+77.50
CTP	12.82±1.13	12.03±1.05	-6.16	4.47±0.84	7.70±3.41	+72.26

Note: Values are tabulated as means ± SD. C, sedentary with placebo control group; CT, exercise group; CTP, combined probiotics with exercise group; IL, interleukin; P, probiotics group.

*Significant difference from pre-test ($p < 0.05$).

In summary, between-group effects showed that interleukin responses and muscular performance were not significantly different between control, probiotics alone, exercise alone, and the combination of probiotics and exercise groups. However, exercise alone significantly increased in most of the immune cells count measured, such as IL-10 concentration, and showed increased muscular strength and power in both dominant and nondominant legs. Probiotics alone significantly increased IL-10 concentration but not the other measured parameters. In addition, this combination also showed significant increases of muscular power and strength in both legs of the participants but the other measured parameters were not significantly affected.

Hence, this study suggests that 12 weeks of circuit training alone and the combination of circuit training and probiotic consumption improved muscular performance while circuit training alone and probiotics alone increased IL-10 concentration.

Conflict of interest statement

The authors have no conflict of interest.

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