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Sport nutrition, redox homeostasis and toxicity in sport performance

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Abstract

The health benefits of exercise are widely accepted and have been used to prevent and treat chronic diseases. Exercise, however, is also associated with production of reactive oxygen and nitrogen species (RONS) which, when in excess, can exert toxic effects such as oxidation of lipids and proteins as well as DNA damage. Because unfavourable effects can be found due to a redox status imbalance, dietary supplementation has been used in an attempt to protect and enhance exercise performance. In this review, we performed a thorough PubMed search for human studies with dietary supplements. We review recent studies on the effects of vitamin C, vitamin E (focussing on the effects of these vitamins during chronic exercise only), polyphenols (resveratrol and green tea extract) and N-acetylcysteine. Furthermore, we present data of the effects of protein supplementation and, more specifically, whey protein, which has drawn attention lately due to its antioxidant properties. Protein ingestion seems to be promising not only by scaling down the redox status perturbations after exercise but also by leading to better exercise performance. How these two are related is something that needs to be determined in future studies. In addition, as diet can modulate the composition of the gut microbiota and a possible crosstalk between the gut and mitochondria might take place, an attempt was made to elucidate the possible role of the gut microbiota on mitochondria-related RONS production during exercise. It seems that exercise could positively influence the human gut microbiota composition by increasing diversity and favouring the increase of relative abundances of health-promoting microbial species. At the moment, it is not clear whether a definite recommendation in favour or avoidance of the reviewed supplements could be made. Supplementation in athletes with deficiencies and in greater need, such as overtraining, is definitely something that needs to be determined in future studies.

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Introduction

The importance of physical activity in modern daily life is very well established, and it is now considered as medicine for a vast majority of chronic diseases [1]. This is due to the health benefits that exercise training provides such as increased oxygen uptake, muscle strength and mass and many others. These physiological adaptive responses are achieved via increases in insulin sensitivity [2], mitochondrial biogenesis [3], protein synthesis [4] and upregulation of endogenous antioxidant defence mechanisms [5].

Exercise is also associated with production of reactive oxygen and nitrogen species (RONS) which, when in excess, can exert toxic effects as they cause oxidation of molecules such as lipids and proteins as well as DNA damage [6]. These disturbances in redox balance result in unfavourable effects on the training adaptive responses such as muscle damage and fatigue [7], which can ultimately result in decreased performance. Therefore, enhancement of the antioxidant defence system by administration of nutritional supplements has been adopted to counteract these deleterious effects of the exercise-induced oxidative damage. This practice has been mainly implemented among professional athletes where athletic performance is crucial. However, dietary supplement consumption in conjunction with an exercise training program has also been increased during the last few decades among recreational athletes or individuals engaged in regular physical activity.

Nevertheless, this is a practice that has been questioned strongly because exercise-induced RONS act also as

signalling molecules for the aforementioned beneficial effects in response to exercise training. RONS produced during muscle contractions are responsible for key adaptations to exercise training as mitochondrial biogenesis [8], endogenous antioxidant enzyme upregulation [9], muscle hypertrophy [10] and glucose uptake by the skeletal muscle [11]. In line with this, the use of supplements with antioxidant properties for ameliorating the exercise-induced RONS increases has grown to a debatable subject as there has been considerable evidence that these supplements might not only prevent the toxic effects of RONS but also blunt their signalling properties responsible for the adaptive responses [12].

A substantial variety of nutritional supplements have been used to test whether they can offer protection and enhancement of exercise performance or whether they might prevent the physiological adaptations to exercise. In this review, we will summarise studies in which the most common dietary antioxidant supplements have been used in relation to either endurance or resistance exercise and their effects on redox status and exercise performance in humans.

Literature search

A thorough PubMed search took place for human studies with the dietary supplements that have been most commonly used. We narrowed our report down to the effects of vitamin C, vitamin E, polyphenols (resveratrol and green tea extract) and N-acetylcysteine. Furthermore, we present data of the effects of protein supplementation and, more specifically, whey protein, which has drawn the attention lately due to its antioxidant properties. In addition, because diet can modulate the composition of the gut microbiota and a possible crosstalk between the gut and mitochondria might take place, an attempt was made to elucidate the possible role of the gut microbiota on mitochondria-related RONS production during exercise.

Finally, as the number of studies that have tested the antioxidant properties of vitamin C and E is immense, we focused on the effects of these vitamins in relation to only chronic exercise and not acute as the latter is required for adaptations to occur.

Repeated endurance exercise leads to increased number and size of mitochondria in the skeletal muscle as well as upregulation of the oxidative enzymes. In addition to that, endurance training results in increased capillary density, antioxidant enzymes and cardiovascular adaptations, for example, increased cardiac output and lower heart rate at rest (Refs. Holloszy et al. [123]; Alexander S., [124]). Therefore, the skeletal muscle becomes more efficient in terms of utilizing oxygen and metabolizing free fatty acids to produce energy during exercise. Consequently, improvement in respiratory and antioxidant capacity, substrate utilization and cardiovascular fitness are achieved, all of which are essential parameters for improving sport performance.

Resistance training is the exercise modality that stimulates skeletal muscle hypertrophy via increases in the cross-sectional area of the individual muscle fibres (Abernethy PJ et al. [125]). Furthermore, neural (Kraemer et al. [126]) and metabolic adaptations (Paschalis et al. [24]) have been noted as adaptive responses to resistance training. These modifications lead to increases in muscle mass and strength, which are also vital assets in athletic performance.

Nutritional supplements, redox status and exercise performance

Effects of vitamin C and E consumption during endurance training on redox status and performance

Vitamin supplements with antioxidant properties are the most widely used compounds against the exercise-induced RONS production. More specifically, vitamins C and E, either separately or in combination, are the two main vitamins that have mostly been used. Therefore, the data presented in this section will be focused on studies that have used the aforementioned vitamins as antioxidant supplements (Table 1).

Most studies that have investigated the relation of vitamin supplementation with exercise have mainly used endurance mode of exercise. The first studies were focused mainly on the effect of the vitamins as ergogenic aid to enhance performance; therefore, data on the redox status were not always available. In 2007, a study was presented which showed that vitamin C and E supplementation administered before an endurance exercise protocol had a positive effect on endurance performance in endurance-trained individuals [13].

However, most studies in which vitamin consumption has been administered during the endurance training period have demonstrated that there is no additive effect of the antioxidants on performance. Zoppi et al. [14] measured aerobic performance and strength in soccer players after a training period with concomitant vitamin C and E supplementation and found that the beneficial training effect was not affected by the vitamin consumption. Numerous studies that followed also demonstrated a clear training effect on maximal oxygen consumption (VO_{2max}) [15–18] and aerobic power measured using submaximal tests [18] which was not impacted by the vitamin supplementation.

Many of these studies investigated, apart from performance, the possible effect on the redox status and other molecular adaptive responses to endurance training, and

Table 1 Effects of vitamin C and E supplementation during endurance or resistance exercise training on performance and redox parameters.

Study	Subjects	Age	Training protocol	Nutritional supplementation protocol	Effect of training/ exercise	Effect of supplementation	Effect of training/ exercise	Effect of supplementation
					Performance		Redox status	
Vitamin C and E — Endurance training								
Aguilo et al. 2007	15 amateur athletes	–	Three months of endurance training	90 days with 500 mg × day (-1) of vitamin E and 30 mg × day (-1) of beta-carotene, and the last 15 days also with 1 g × day (-1) of vitamin C	↑ VO_2max	↓ Max blood [lactate]	–	
Zoppi et al. 2006	10 male professional soccer players	18 ± 1 yrs	90 days combination of aerobic, anaerobic and strength training	90 days. SG: 1000 mg of Vit C (ascorbic acid) and 800 mg of Vit E (α-tocopherol) daily; Placebo	↑Aerobic capacity ↑Strength ↔Speed	No effect	↔ CAT activity ↔ Glutathione reductase activity ↔ Carbonyls	↔ CAT activity ↔ Glutathione reductase activity ↔ Carbonyls ↓TBARS ↓CK
Yfanti et al. 2010	21 physically active males	18–40 yrs	12 weeks of endurance training (heavy cycling), 5 days/week.	16 weeks (4 weeks preloading). SG: 500 mg of Vit C (ascorbic acid) and 400 IU Vit E (α-tocopherol) daily; Placebo	↑VO_2max ↑Maximal power ↑Skeletal muscle glycogen concentration ↑Mitochondrial enzyme activity (CS, β-HAD)	No effect	↑MnSOD	No effect
Morrison et al. 2015	11 males	18–35 yrs	4 weeks of endurance training (cycling), 3 days/week	8 weeks (4 weeks preloading). SG: 1000 mg of Vit C and 400 IU Vit E daily; Placebo	↑VO_2peak ↔PGC-1α mRNA ↑TFAM protein ↑COX4 mRNA and protein ↑Mitochondrial enzymes (CS)	No effect	↔ F_2-isoprostanes ↔ GSSG ↑GSH ↑GPx1 mRNA ↑SOD mRNA and protein	↓SOD enzymatic activity
Paulsen et al. 2014	54 males and females (recreationally endurance trained)	–	11 weeks of endurance training (running), 3–4 days/week	11 weeks. SG: 1000 mg of Vit C and 235 mg of Vit E daily; Placebo	↑VO_2max ↑Running performance (20-m shuttle run test)	↓Mitochondrial biogenesis (COX4, PGC-1α, CDC42 and MAPK1)	No effect	No effect
Gomez-Cabrera et al. 2008	14 sedentary males	–	8 weeks of endurance training (cycling), 3 days/week	8 weeks. SG: 1000 mg of Vit C daily; Placebo	↑VO_2max	No effect	–	–
Ristow et al. 2009	40 males	25–35 yrs	4 weeks of endurance and strength training, 5 days/ week	4 weeks. SG: 1000 mg of Vit C and 400 IU Vit E daily; Placebo	↑Mitochondrial biogenesis (PGC-1α, PGC-1β and PPARγ)	↓Mitochondrial biogenesis (PGC-1α, PGC-1β and PPARγ)	↑TBARS ↑SOD1 mRNA ↑SOD2 mRNA ↑GPX1 mRNA	↓TBARS ↓SOD1 mRNA ↓SOD2 mRNA ↓GPX1 mRNA

(*continued on next page*)

Table 1. (*continued*)

Study	Subjects	Age	Training protocol	Nutritional supplementation protocol	Effect of training/ exercise	Effect of supplementation	Effect of training/ exercise	Effect of supplementation
					Performance		Redox status	
Yfanti et al. 2012	21 physically active males	18–40 yrs	12 weeks of endurance training (heavy cycling), 5 days/week.	16 weeks (4 weeks preloading). SG: 500 mg of Vit C (ascorbic acid) and 400 IU Vit E (α-tocopherol) daily; Placebo	–	–	↑MDA (skeletal muscle) ↑Protein carbonyls	↑MDA (skeletal muscle) ↑Protein carbonyls ↑CuZnSOD mRNA ↑GPx1 mRNA
Vitamin C and E — Resistance training								
Theodorou et al. 2011	28 recreationally trained males	–	4 weeks of eccentric training, 2 days/ week	9 weeks (5 weeks preloading). SG: 1000 mg of Vit C (ascorbic acid) and 400 IU Vit E (D-α-tocopherol) daily; Placebo	↑Muscle function ↑Muscle performance	No effect	↑GSH ↔GSSG ↓Carbonyls ↓TBARS	No effect
Bobeuf et al. 2011	57 sedentary males and females	65.6 ± 3.8 yrs	6 months of resistance training, 3 days/ week	6 months. SG: 1000 mg of Vit C and 400 IU Vit E daily; Placebo; Supplemented + resistance exercise; Resistance exercise	↑Muscle mass ↑Strength	No effect	↔MDA ↔F_2-isoprostanes ↔TAS	↔MDA ↔F_2-isoprostanes ↔TAS
Paulsen et al. 2014	32 recreationally trained males and females	–	10 weeks of resistance training, 4 days/ week	10 weeks. SG: 1000 mg of Vit C and 235 mg of Vit E daily; Placebo	↑Muscle strength ↑Muscle mass ↑Muscle hypertrophy (in response to acute exercise)	↓Increase in muscle strength ↓Muscle hypertrophy (in response to acute exercise)	–	–
Bjørnsen et al. 2016	34 elderly males	60–81 yrs	12 weeks of resistance training, 3 days/ week	12 weeks. SG: 1000 mg of Vit C and 235 mg of Vit E daily; Placebo	↑Muscle thickness (v.lateralis) ↑Muscle strength ↑Lean mass	↓Muscle thickness (v.lateralis) ↑Muscle strength ↓Increase in lean mass	–	–

SG: supplemented group; CAT: catalase; TBARS: thiobarbituric acid reactive substances; CK: creatine kinase; CS: citrate synthase; β-HAD: β-hydroxyacyl CoA dehydrogenase; PGC-1α: peroxisome proliferator–activated receptor gamma coactivator 1-alpha; TFAM: mitochondrial transcription factor A; COX4: cytochrome *c* oxidase; GSH: reduced glutathione; GSSG: oxidised glutathione; GPx1: glutathione peroxidase 1; CDC42: cell division control protein 42; MAPK1: mitogen-activated protein kinase 1; PPARγ: Peroxisome proliferator-activated receptor gamma; MDA: malonaldehyde; TAS: total antioxidant status.

the results are somewhat confusing. Ristow et al., in 2009 [19], reported that supplementation with vitamin C and E during 4 weeks of training hampers the training-induced adaptive responses with regards to markers of mitochondrial biogenesis and the antioxidant enzymes superoxide dismutase (SOD) and glutathione peroxidase 1 (GPX1). Some years later, Paulsen et al. [18] confirmed the detrimental effects of vitamin consumption during endurance training on mitochondrial biogenesis. Furthermore, Morrison et al. [16] reported an increase of the antioxidant enzyme SOD in response to the endurance training which was attenuated by the antioxidant supplementation. The same detrimental effect of the vitamins was not, however, present on most of the markers of mitochondrial biogenesis in this study.

In addition, in a large endurance training study that we performed some years earlier [20], although we did not find any differences between the supplemented and the placebo group on performance parameters, we detected an overall increase of oxidative stress markers in the group that consumed vitamins C and E during training. This increase was also accompanied by higher mRNA expression of the antioxidant enzymes CuZnSOD and GPX1 which, however, was not translated to increases in protein content.

Taken together, it becomes obvious that supplementation with vitamins C and E during endurance training might cause an increased toxicity in the cellular environment and interfere with the exercise-induced adaptive responses on a molecular level. However, these changes do not seem to be translated to changes in endurance performance. Nevertheless, it is very difficult to draw concrete conclusions as the studies that have investigated this hypothesis differ extensively in methodology. In addition, in most of these studies, the population consists of young healthy individuals with an overall high fitness level. It might therefore be the case that the beneficial effect of endurance training in an already healthy population might be adequate to overrule any possible effects of the vitamin supplementation.

Effects of vitamin C and E consumption during resistance exercise training on redox status and performance

Although most studies that have investigated the interrelation of vitamin C and E supplementation and exercise have focused on endurance mode of exercise, a few studies have emerged during the last decade which focused on the effects of antioxidant supplementation during resistance exercise on adaptive responses. Resistance exercise is essential for maintaining and increasing muscle mass [4] which is vital for good health and also for increasing physical performance. As resistance exercise is also associated with increased toxicity due to muscle damage and RONS production, it was logical for investigators in the field to investigate the effect of antioxidant supplementation and resistance exercise on performance and redox status.

In 2011, our group published a thorough study in which the effects of concomitant consumption of vitamins C and E and resistance exercise training on muscle performance and redox status in young healthy individuals were examined [21]. The mode of exercise used here was eccentric exercise that has been shown to induce muscle damage and changes in the redox status [22–24]. The training consisted of 4 weeks of eccentric exercise training while subjects were supplemented with vitamins C and E. The training increased the parameters of muscle performance; however, the supplementation did not appear to have any additive effect. The same lack of effect of the antioxidant vitamins was present on markers of redox status. The chronic exercise protocol seemed to increase the antioxidant potential as revealed from markers measured both in the blood and skeletal muscle. Nevertheless, the vitamin C and E consumption did not seem to interfere with these responses. The same year, Bobeuf et al. [25] reported the results from a study in which elderly individuals were supplemented with vitamins C and E for 6 months while performing resistance training. They also did not find any significant impact of the vitamins on muscle strength or the antioxidant/prooxidant balance.

A couple of years later, Paulsen et al. [26] changed the notion of the lack of effect of antioxidant vitamins on resistance training–induced adaptive responses in healthy young individuals. They performed a training study with traditional resistance exercises during which participants were consuming vitamins C and E daily. Vitamin consumption partly attenuated the increases in muscle strength after the training period, whereas there were no differences between the groups with regards to increases in muscle mass. The authors also performed an acute bout of resistance exercise in the middle of the training period during which they tested the effect of exercise and antioxidant supplementation on the signalling pathways associated with skeletal muscle hypertrophy. The results revealed that vitamin supplementation clearly prevented the upregulation of hypertrophy markers in skeletal muscle. Two years later, the same group presented data from a similar study performed in elderly individuals [27]. Although the supplementation did not affect the increases in muscle strength after the training period, it impaired the expected training-induced increase in total lean mass and muscle thickness of specific muscle groups of the elderly individuals.

Although markers of redox status were not reported in the latter two studies [26,27], it can be speculated that

as there were pronounced effects of the nutritional supplements on the signalling pathways in the skeletal muscle and some of the physiological parameters, the vitamins have probably caused a disturbance in the cellular redox balance. Nonetheless, these alterations were only partly translated in alterations in physiological parameters measured.

Effects of supplementation with polyphenols during exercise training on redox status and performance

Polyphenols are a group of phytochemicals that have received great attention of researchers in the past decades due to their beneficial effects in the prevention of many chronic diseases [28,29]. Polyphenols are present in fruits, vegetables and grains and have strong antioxidant capacities. Therefore, it has been hypothesized that supplementation with polyphenols or polyphenol-rich diets will exert protective effects against chronic diseases that are characterized by high levels of oxidative stress, namely, cardiovascular diseases, cancer and chronic inflammation [30].

The most widely used polyphenols that have been used as supplements in relation to exercise-induced oxidative stress are resveratrol and catechins. Therefore, the data presented in this review are focused on these compounds (Table 2).

Resveratrol

Resveratrol is a polyphenolic compound that is present in various plants such as grapes, berries, nuts and plums and also abundant in commercial products such as red wine. Resveratrol supplementation has gained a great interest in the past decades due to the notion that it probably contributes to the 'French paradox' which refers to the fact that the prevalence of cardiovascular disease in France is low although they are accustomed to a diet rich in saturated fat [31]. This paradox may be attributable to the high consumption of red wine in France. Resveratrol exerts strong antioxidant capacities via different mechanisms, either by directly scavenging free radicals or by stimulating the upregulation of endogenous antioxidant defence mechanisms [32]. Therefore, it has been speculated that resveratrol may offer protection against the toxic effects of exercise-induced oxidative stress.

The number of human studies with concomitant exercise and resveratrol supplementation are sparse, and the results are equivocal. Some years ago, Gliemann et al. [33] conducted a study in which elderly individuals consumed resveratrol supplements during an 8-week high-intensity exercise training period. The mode of exercise used here was a combination of aerobic and resistance exercise. The results showed that resveratrol had detrimental effects on the beneficial training-induced increases in maximal oxygen consumption and on some of the metabolites. Despite these negative effects, the nutritional protocol did not affect the antioxidant defence mechanisms. The same group, in a similar study with the same elderly population [34], also demonstrated that resveratrol supplementation blunted the reduction in oxidative stress and inflammation that occurred with training alone. However, there was no additive effect of the resveratrol on markers of mitochondrial biogenesis and on oxidative enzymes.

The same year, another study was published by Scribbans et al. [35] in which resveratrol supplementation was given to young healthy individuals during a 4-week high-intensity training program. Their results were partly in agreement with those by Gliemann et al. [33] as the authors found a blunting effect of resveratrol on peak aerobic power and in upregulation of antioxidant enzymes. Furthermore, it was also demonstrated that markers of mitochondrial biogenesis were attenuated in the supplemented group, an effect that was in contrast with the one described by Olesen et al. [34].

Nevertheless, there are recent studies that contradict the aforementioned toxic effects of resveratrol on training adaptations. Polley et al. [36] found that resveratrol supplementation during submaximal endurance training of the wrist flexor muscles increases mitochondrial capacity. Furthermore, Alway et al. [37] also showed that the polyphenolic compound had positive effects in VO_{2max}, muscle strength, muscle power and mitochondrial volume density when used during a 12-week endurance and resistance training program in elderly individuals.

Finally, only one study examined the long-term effect of resveratrol (100 mg/day for 90 days) on redox response to acute exercise in military firefighters [38]. The results revealed that the exercise protocol failed to cause any changes in the tested indices of redox status and no effect of resveratrol supplementation was evident.

It is obvious that the existing human data on the effects of resveratrol on exercise-induced adaptations are controversial and therefore, it becomes very difficult to draw definitive conclusions. It must be taken into account that only 70–75% of resveratrol after oral administration in humans is absorbed and that it has a rapid metabolism, mainly by the intestine and liver [39]. This results in very low bioavailability of resveratrol which could be one potential reason for the ambiguous results after resveratrol supplementation. There is certainly still room for further research in this field before recommendations for supplementation with resveratrol during exercise can be made.

Table 2 Effect of polyphenols supplementation during exercise or training on performance and redox parameters.

Study	Subjects	Age	Training/Exercise protocol	Nutritional supplementation protocol	Effect of training/ exercise	Effect of supplementation	Effect of training/ exercise	Effect of supplementation
					Performance		Redox status	
Resveratrol								
Gliemann et al. 2013	27 physically inactive males	65–72 yrs	8 weeks of high-intensity endurance (cycling, 2 days/week + circuit training 1 day/week	8 weeks. SG: 250 mg RSV/day; Placebo	↑VO_{2max} ↓Mean arterial blood pressure	↓VO_{2max} ↔Mean arterial blood pressure	↑SOD2 ↑NOX ↔CAT ↔GPX1 ↔SOD1	↑SOD2 ↑NOX ↔CAT ↔GPX1 ↔SOD1
Olesen et al. 2014	43 physically inactive males	60–72 yrs	8 weeks of high-intensity endurance (cycling, 2 days/week + circuit training, 1 day/ week + walk 5 km, 1 day/week	8 weeks. SG: 250 mg RSV/day; Placebo (PL); RSV+ exercise; PL+exercise	↑Muscle endurance ↑PGC-1α mRNA ↑CS ↑HAD ↑cyt *c* protein ↑COX1 ↓TNF-α mRNA	↑Muscle endurance ↑PGC-1α mRNA ↑CS ↑HAD ↑cyt *c* protein ↑COX1 ↔TNF-α mRNA	↓Protein carbonyls	↔Protein carbonyls
Scribbans et al. 2014	16 recreationally active males	22 yrs	4 weeks interval cycling exercise, 3 days/week	4 weeks. SG: 150 mg RSV/day; Placebo.	↑VO_{2peak} ↑Peak aerobic power ↑PGC-1α mRNA ↑SIRT1 mRNA	↑VO_{2peak} ↔Peak aerobic power ↔PGC-1α mRNA ↔SIRT1 mRNA	↑SOD2 mRNA ↑GPx1 mRNA	↔SOD2 mRNA ↑GPx1 mRNA
Polley et al. 2016	16 healthy	–	4 weeks of submaximal endurance training, 3 days/week	4 weeks. SG: 500 mg RSV/day + 10 mg piperine; Placebo.	↔Mitochondrial capacity (skeletal muscle)	↑Mitochondrial capacity (skeletal muscle)		
Alway et al. 2017	30 elderly males and females	65–80 yrs	12 weeks of combined endurance and resistance training	12 weeks. SG: 500 mg RSV/day; Placebo	↔VO_{2max} ↔Muscle strength ↔Muscle function ↔Mitochondrial density	↑VO_{2max} ↑Muscle strength ↑Muscle function ↑Mitochondrial density	–	–
Macedo et al., 2015	60 military firefighters	Resveratrol (n = 30): 21.5 ± 1.8 yrs; placebo (n = 30): 22.3 ± 1.8 yrs	Fitness test consisting of 4 exercises: (1) chin-up, (2) abdominal sit-up, (3) speed test: 50 m sprint; (4) aerobic exercise: running for 12 min (Cooper test)	90 days. 100 mg RSV/day	–	–	–	No change
Green tea - Acute exercise								
Panza et al. 2008	14 recreationally trained males	19–30 yrs	1 resistance exercise bout	7 days before the acute exercise: 600 ml of green tea/day; Placebo	–	–	↔Polyphenols ↔FRAP ↔Hypoxanthine ↔Uric acid ↑XO ↑CK ↑Lipid hydroperoxides ↓GSH	↑Polyphenols ↑FRAP ↑Hypoxanthine ↑Uric acid ↔XO ↔CK ↔Lipid hydroperoxides ↑GSH
Eichenberger et al. 2010	9 endurance-trained cyclists	32.2 ± 2.1 yrs	1 endurance exercise bout (cycling)	21 days before the acute exercise: 159 mg of total catechins/day; Placebo	↔CRP	↓CRP	–	–

(*continued on next page*)

Table 2. (*continued*)

Study	Subjects	Age	Training/Exercise protocol	Nutritional supplementation protocol	Effect of training/ exercise	Effect of supplementation	Effect of training/ exercise	Effect of supplementation
					Performance		Redox status	
Eichenberger et al. 2009	9 endurance-trained cyclists	–	1 endurance exercise bout (cycling)	21 days before the acute exercise: 160 mg of total catechins/day; Placebo	↔CK ↔HDL	↓CK ↑HDL	No change	No change
Suzuki et al. 2015	9 well-trained male cyclists	–	1 endurance exercise bout (cycling)	2 times × 22 mg/kg body mass of catechins + 6 mg/kg body mass of caffeine + 230 mg/kg of glucose + 110 mg/kg of fructose; Placebo: 2 times × 230 mg/kg body mass of glucose + 110 mg/kg body mass of fructose	No effect	No effect	–	–
Jówko et al. 2015	16 male sprinters	21.6 ± 1.5 yrs	1 endurance exercise bout (cycling)	4 weeks before acute exercise: 1000 mg of green tea extract/day; Placebo	↑CK	↑CK	↔Total polyphenols ↔TAC ↑SOD ↔GPx ↑MDA	↑Total polyphenols ↑TAC ↓SOD ↔GPx ↑MDA
Jówko et al. 2012	16 soccer players	–	1 resistance exercise bout	Single dose of 640 mg of green tea polyphenols; Placebo	↑CK	↑CK	↑TBARS ↑Uric acid ↑TAS ↔SOD	↑TBARS ↑Uric acid ↑TAS ↔SOD
Sugita et al. 2016	16 physically active males	20–23 yrs	1 endurance exercise bout (cycling)	Single dose of 780 mg of green tea catechins; Placebo			↑d-ROMS ↑BAP ↑8-OHdG	↑d-ROMS ↑BAP ↑8-OHdG
Chronic exercise								
Jówko et al. 2011	35 healthy males	–	4-week of resistance training, 3 days/week	4 weeks. SG: 640 mg of green tea/day; Placebo	↑Muscle strength	↑Muscle strength	↑Lipid peroxidation ↔Total polyphenols ↔TAS	↔Lipid peroxidation ↑Total polyphenols ↑TAS
Kuo et al. 2015	40 healthy males	20 ± 1 yrs	4 weeks of endurance training, 3 days/week	4 weeks. Control; GTE 250 mg/day+training; GTE 250 mg/day; Training only	↑Endurance exercise capacity ↑CK	↑Endurance exercise capacity ↔CK	↔TAS ↑MDA (in response to acute exercise)	↑TAS ↔MDA (in response to acute exercise)
Narotzki et al. 2013	22 elderly males and females	71.1 ± 1.2 yrs	12 weeks of endurance training, 6 days/week (walking)	12 weeks. SG: 3 cups of green tea + 400 IU vitamin E; Placebo	↑Exercise capacity ↔Waist circumference ↔Glucose	↑Exercise capacity ↓Waist circumference ↓Glucose	↔Protein carbonyls ↔CAT activity	↓Protein carbonyls ↑CAT activity
Roberts et al. 2015	14 recreationally active males	21.4 ± 0.3 yrs	3 endurance of exercise trials at weeks 0, 2 and 4.	4 weeks. SG: 571 mg/day; Placebo	↔Fat utilization ↔Glucose utilization ↔Heart rate ↔Exercise performance (distance covered) ↔Power output	↑Fat utilization ↓Glucose utilization ↓Heart rate ↑Exercise performance (distance covered) ↑Power output	–	–

Qian et al. 2012	171 females with osteopenia	6 months of Tai Chi exercise, 3 days/week	6 months. SG: 500 mg of green tea polyphenols/day; Placebo (PL); SG+exercise; PL+exercise	↓8-OHdG	↓8-OHdG

8-OHdG: 8-hydroxydeoxyguanosine; SG: supplemented group; RSV: resveratrol; SOD: superoxide dismutase; CAT: catalase; NOX: NADPH oxidase; GPx: glutathione peroxidase; PGC-1α: peroxisome proliferator–activated receptor gamma coactivator 1-alpha; CS: citrate synthase; HAD: hydroxyacyl CoA dehydrogenase; COX: cytochrome *c* oxidase; TNFα: tumour necrosis factor-alpha; SIRT1: sirtuin1; FRAP: ferric-reducing ability of plasma; XO: xanthine oxidase; CK: creatine kinase; GSH: reduced glutathione; CRP: C-reactive protein; HDL: high-density lipoprotein; TAC: total antioxidant capacity; MDA: malondialdehyde; TBARS: thiobarbituric acid reactive substances; TAS: total antioxidant status; d-ROMS: diacron reactive oxygen metabolites; BAP: biological antioxidant potential.

Catechins (green tea extract)

One of the main categories of catechins, a type of polyphenols, is the green tea extract, consumption of which has been reported to exert many health benefits in relation to diseases associated with increased free radical production and oxidative stress [40]. Therefore, owing to these antioxidant properties, the role of green tea extract as an antioxidant supplement against the exercise-induced oxidative stress has been the focus of several studies in recent years.

The effects of green tea extract were initially studied in response to an acute bout of exercise, either resistance or aerobic exercise. Panza et al. [41] evaluated the effect of a 7-day prior supplementation with green tea extract on redox balance after an acute bout of resistance exercise, and they reported increased antioxidant potential as noted by increased total antioxidant capacity and plasma polyphenols and reduced glutathione and also reduced lipid peroxidation, xanthine oxidase activity and creatine kinase. The same pronounced beneficial effects though were not as evident as when catechins were injected for three weeks before an acute bout of endurance exercise [42,43]. The investigators detected a beneficial effect with regards to inflammation and muscle damage markers; however, there was no effect on oxidative stress markers or performance of the endurance-trained participants. In addition, when green tea was consumed during recovery from sprint exercise [44], it did not seem to provide any antioxidant or antiinflammatory effect. Furthermore, this supplementation protocol did not affect sprint cycling performance either. Jowko et al. [45], however, reported that when green tea extract was consumed for 4 weeks by sprint athletes before they performed a single bout of sprint tests, it prevented oxidative stress. Nevertheless, even this longer supplementation protocol was not adequate to increase performance or to prevent muscle damage. The aforementioned research group tested also the effect of a single injection of green tea polyphenols before an acute resistance exercise protocol to exhaustion in soccer athletes, and they found that a single shot does not offer any protection against oxidative toxicity or muscle damage [46]. Sugita et al. [47] reached the same conclusion when they administered a single shot of catechins during a single endurance exercise bout to exhaustion.

There are a substantial number of studies that have also focused on the interrelation between green tea extract supplementation and changes in redox balance and adaptations after chronic exercise. Jowko et al. [48] performed a 4-week resistance training study in young healthy individuals, and they observed that the supplementation provides protection against the exercise-induced oxidative toxicity while at the same time enhancing the antioxidant potential at rest as evidenced by prevention of lipid peroxidation and increased plasma

polyphenols. Beneficial effects of green tea extract supplementation have also been reported after chronic endurance training in antioxidant capacity [49,50], performance [51] and glucose tolerance [50]. More specifically, Kuo et al. [49] and Roberts et al. [51] adopted a 4-week endurance exercise protocol in young untrained or recreationally active men, respectively, and they found that the concomitant green tea extract supplementation exerted beneficial effects by preventing increases in markers of oxidative damage and enhancing antioxidant capacity after the training period and in response to acute exercise [49]. Furthermore, the results of the study by Roberts et al. [51] demonstrate an overall increase in performance indices, namely, power output, distance covered during submaximal exercise, heart rate and increased substrate utilisation after the combined supplementation and training intervention.

Narotzki et al. [50] applied a longer training protocol in elderly men and women where they also administered vitamin E in addition to the green tea extract. The 12-week intervention significantly improved body composition and glucose tolerance of the elderly individuals while it also exerted positive results against oxidative damage. Furthermore, in the study by Qian et al. [52], administration of 500 mg of green tea polyphenols during a 6-month Tai Chi exercise training program was also adequate to decrease DNA damage in postmenopausal women with osteopenia, providing a protective effect against oxidative damage in this specific population.

Effects of supplementation with N-acetylcysteine during exercise or training on redox status and performance

N-acetylcysteine (NAC) is a thiol donor with antioxidant properties and potential ergogenic effects. NAC has been used as a nutritional supplement and a pharmaceutical drug in the treatment of various diseases associated with oxidative stress. Moreover, NAC has been proposed to protect against exercise-induced oxidative stress, which may result in improved exercise performance and delayed muscle fatigue [53]. However, as it was eluded earlier, exercise-induced oxidative stress in the working skeletal muscle may be essential for exercise adaptations, and therefore, it is not clear whether NAC supplementation is an appropriate strategy to enhance exercise performance (Table 3).

Research on the effect of acute oral NAC supplementation on redox homeostasis and exercise performance is scarce. Ferreira et al. [54] examined the effect of oral administration of NAC on plasma thiols, handgrip exercise performance and adverse reactions. Seventeen healthy subjects (age: 30 ± 2 years) participated in a double-blinded, placebo-controlled, crossover design study. Participants received NAC in capsules [0 mg (placebo), 300 mg and 600 mg) or solution [0.9% saline (placebo), 35, 70 and 140 mg/kg body mass], and then they performed a handgrip exercise test. NAC solution increased plasma reduced glutathione (GSH) and cysteine levels and decreased GSSG levels compared to placebo in a dose−response manner. Increased cysteine-to-total cysteine ratio was also observed and was directly related to handgrip exercise performance. It was concluded that 70 mg/kg of NAC solution was the optimum dose for obtaining favourable changes in plasma thiols and improved exercise performance without causing significant adverse reactions.

A more recent study [55] investigated the effect of acute NAC supplementation on limb blood flow and muscle oxygenation characteristics during severe-intensity exercise. Eight healthy non-endurance-trained males (age: 21.8 ± 1.2 years) participated in a randomized double-blind placebo-controlled crossover design study. Participants received either NAC (70 mg/kg body mass) or placebo pills, and 1 h later, they performed a handgrip exercise test at 80% peak power to exhaustion. Immediately before exercise, plasma cysteine and total cysteine increased significantly after NAC supplementation compared to placebo; however, plasma redox status was not measured during or after exercise and no conclusion can be made about the efficacy of NAC. Nevertheless, time to exhaustion, blood flow, vasodilation and muscle oxygenation characteristics did not significantly differ between NAC and placebo at any time point. One possible explanation for the lack of changes in exercise performance after NAC supplementation could be that because participants were healthy, they exhibited low levels of oxidative stress. Therefore, NAC supplementation may be more effective when oxidative stress occurs.

There is a greater interest in the investigation of the short-term effects of oral NAC supplementation on redox status and exercise performance; however, these effects and their association have not been well investigated. Silva et al. [56] investigated the effect of short-term NAC supplementation (capsules containing 10 mg/kg body mass) on indices of oxidative damage and inflammatory response after high-intensity eccentric exercise to exhaustion. Twenty-nine healthy males (age: 21.3 ± 4 years) were randomly assigned to one of three groups: NAC (14 days before and 7 days after exercise; n = 9), NAC plus placebo (14 days of NAC before exercise and 7 days of placebo after exercise; n = 8) or placebo (14 days before and 7 days after exercise; n = 8). Fourteen days after starting supplementation, all participants performed an exercise protocol consisting of 3 sets of elbow flexion and extension using 80% of their one-repetition maximum (1-RM). No effect of NAC on indices of oxidative damage (as indicated by malondialdehyde [MDA] and protein carbonyls) and muscle soreness was observed. Tumour necrosis factor-alpha

Table 3 Effect of NAC supplementation during exercise or training on performance and redox parameters.

Study	Subjects	Age	Training protocol	Nutritional supplementation protocol	Effect of training/ exercise	Effect of supplementation	Effect of training/ exercise	Effect of supplementation
					Performance		Redox status	
NAC								
Ferreira et al., 2011	17 health individuals	30 ± 2 yrs	Handgrip test	NAC: 0 mg (placebo), 300 mg and 600 mg) or solution [0.9% saline (placebo), 35, 70 and 140 mg/kg BM	–	70 mg/kg BM of NAC solution for obtaining favourable changes without causing significant adverse reactions	–	NAC solution vs placebo (in a dose–response manner): ↑GSH ↑GSH/GSSG ↑cysteine ↓GSSG levels
Smith et al., 2016	8 healthy non-endurance-trained males	21.8 ± 1.2 yrs	Handgrip test	NAC: 70 mg/kg BM	–	No change	–	- Resting levels: ↑cysteine ↑total cysteine
Silva et al., 2008	29 healthy males	21.3 ± 4 yrs	High-intensity eccentric exercise to exhaustion; elbow flexion and extension; 80% of 1-RM	NAC: 10 mg/kg BM (14 days before and 7 days after exercise; n = 9), and NAC plus placebo (14 days of NAC before exercise and 7 days of placebo after exercise; n = 8) or placebo (14 days before and 7 days after exercise; n = 8)	–	–	–	No change
Zembron-Lacny et al., 2009	55 healthy and trained males	21.9 ± 1.7 yrs	Three exercises in a circuit fashion; shoulder press, bench press and deadlift without any breaks; increasing load	NAC: 1.8 g/day; α-lipoic acid: 1.2 g/day; taurine: 3 g/day; placebo	–	–	–	NAC vs placebo: - Resting levels: ↑TAC, ↑TT, ↓TBARS, ↓PC - After exercise: ↑TT, ↓PC
Zembron-Lacny et al., 2010	50 healthy males	20.3 ± 2.3 yrs	Incremental and progressive exercise test to exhaustion; cycle ergometer	NAC: 1.2 g/day for 8 days before and 600 mg on the day of exercise trial, or placebo	–	No change	–	- Resting levels: ↑GSH, ↑TT, ↓glutathione reductase, ↓glutathione peroxidase; ↓PC, ↓TBARS - After exercise: ↑GSH
Leelarungrayub et al., 2011	29 sedentary males		Graded exercise treadmill test (VO_{2max}); %FI of the dominant quadriceps muscle	NAC (n = 16): 1.2 g/day for 7 days or placebo (n = 13)	–	↑VO_{2max} (mL/kg/mL), ↑%FI	–	NAC: - After exercise: No change in TAC Placebo: - After exercise: ↓TAC
Slattery et al., 2014	10 well-trained male triathletes	23.6 ± 3.2 yrs	Cycle ergometer exercise test (race simulation)	NAC: 1.2 g/day for 9 days, or placebo	–	↑sprint performance	–	NAC: - After exercise: ↑TAC, ↓TBARS, ↓urinary 15-isoprostane F_{2t}
Trewin et al., 2013	9 well-trained male cyclists	28 ± 6 yrs	High-intensity interval exercise and 10-min time trial	NAC (200 mg/kg BM for two days before exercise trial and 100 mg/kg BM 30 min preceding exercise trial) or placebo	–	–	–	NAC: - No change in GSH or GSSG at any time point - Resting levels: ↓MDA - During exercise: ↑MDA compared to resting levels in NAC and placebo
Michailidis et al., 2013		23.5 ± 2.5 yrs			–		–	

(*continued on next page*)

Table 3. (*continued*)

Study	Subjects	Age	Training protocol	Nutritional supplementation protocol	Effect of training/ exercise	Effect of supplementation	Effect of training/ exercise	Effect of supplementation
					Performance		Redox status	
	10 recreationally trained males		Muscle-damaging exercise (300 eccentric contractions)	NAC: 20 mg/kg BM for 8 days or placebo		Exercise performance was completely recovered only in the placebo group after 8 days		NAC: - After exercise at various time points: Lower↑ in GSSG, PC and TBARS and lower ↓in GSH - Throughout recovery: ↑GSH/GSSG

NAC: N-acetylcysteine; BM: body mass; GSH: reduced glutathione; GSSG: oxidised glutathione; 1-RM: one-repetition maximum; TAC: total antioxidant capacity; TT: total thiols; TBARS: thiobarbituric acid reactive substances; PC: protein carbonyls; FI: fatigue index; MDA: malondialdehyde.

(TNF-α) increased at the 2nd day after exercise in all groups and remained high at the 4th day after exercise only in the supplemented groups. Moreover, interleukin-10 increased at the 4th day after exercise in all groups and remained high at the 7th day after exercise only in the supplemented groups, indicating a beneficial antiinflammatory effect of NAC. From these results, it cannot be concluded, however, that NAC could protect against muscle soreness. Different exercise and supplementation protocols with more indices examined could provide more information.

In 2009, Zembron-Lacny et al. [57] compared the effects of three-day supplementation with three sulphur-containing compounds on plasma indices of antioxidant status and oxidative damage after muscle-damaging exercise. Fifty-five healthy and trained males were randomly assigned to NAC (1.8 g/day), α-lipoic acid (1.2 g/day), taurine (3 g/day) and control group and performed an intense resistance exercise test that caused muscle damage as indicated by changes in creatine kinase (CK). Three-day supplementation with NAC resulted in increased total thiols before and immediately after exercise. NAC supplementation resulted also in increased total antioxidant status and decreased thiobarbituric acid reactive substances (TBARS) before and immediately after exercise and during recovery (24 h after exercise) compared to the control group. Moreover, protein carbonyls were significantly lower before exercise and during recovery in the NAC supplementation group than in the control group. Finally, NAC supplementation resulted in decreased CK release from skeletal muscle immediately after exercise and also prevented the increase in uric acid during recovery. These results indicate that three-day supplementation with NAC improved plasma total antioxidant status and decreased oxidative damage in healthy males after muscle-damaging exercise.

One year later, another study by Zembron-Lacny et al. [58] examined the effect of NAC supplementation on haematological and redox status indices and exercise performance. Fifteen healthy males were randomly assigned to NAC (1200 mg/day for 8 days before and 600 mg on the day of exercise trial) or control. All participants performed an exercise protocol incorporating an incremental and progressive structure and consisting of three exercises in a circuit fashion. Although NAC supplementation influenced favourable changes in several haematological and redox status indices (before exercise, immediately after exercise and after 24 h of rest), it did not enhance exercise performance.

The same dose of NAC (1200 mg/day) was administered in another study for 7 days, and muscle fatigue, VO_{2max}, total antioxidant capacity (TAC), lactate, CK and TNF-α were examined [59]. Twenty-nine sedentary males were randomly assigned to NAC (n = 16) or placebo

(n = 13) group. All participants performed a graded exercise treadmill test before and after supplementation where VO_{2max} and fatigue index (FI) was evaluated. Moreover, blood samples were taken before and 20 min after each exercise test. Before treatment, TAC levels decreased, whereas lactate, CK and TNF-α levels increased after exercise in both groups. After treatment, exercise resulted in increased CK and TNF-α in both groups, decreased TAC in the control group and no change in TAC and lactate in the NAC group. These results, along with the observation that NAC supplementation increased VO_{2max} and FI, indicate that NAC may have antioxidant effects that lead to improved muscle fatigue and exercise performance. However, more indices of blood redox status would provide additional information and result in a more concise and clear picture.

Slattery et al. [60] also investigated the effect of the same dose of NAC (1200 mg/day) on indices of redox status and cycling performance, this time for 9 days. Ten well-trained male triathletes participated in the investigation in a double-blind randomized placebo-controlled crossover design study. Participants received NAC supplementation or placebo for 9 days; they performed a cycle ergometer exercise test (race simulation) before and after each condition. After exercise, NAC resulted in increased plasma TAC, reduced oxidative damage (as indicated by plasma TBARS and urinary 15-isoprostane F_{2t}), attenuated inflammation (as indicated by plasma interleukin-6 and monocyte chemotactic protein) and increased nuclear factor κB (NFκB) activity. Moreover, NAC supplementation improved sprint performance, which could be associated with the aforementioned improvement in redox status indices.

Trewin et al. [61] investigated the effects of NAC supplementation on metabolism during high-intensity interval exercise (HIIE) and 10-min time trial (TT10). Nine well-trained male cyclists participated in a double-blind, repeated-measures, randomised crossover design study. Participants performed two exercise trials. Before each trial, they received either placebo or NAC (200 mg/kg body mass for two days before exercise trial and 100 mg/kg body mass 30 min preceding exercise trial). Regarding blood redox status, NAC supplementation caused no change in GSH or oxidised (GSSG) glutathione levels compared to placebo at any time point (at rest, exercise or recovery). Plasma lipid peroxidation decreased as indicated by MDA levels in plasma with NAC supplementation at rest; however, MDA increased during HIIE compared to resting levels in both conditions (NAC and placebo). Although NAC caused changes in other parameters of exercise performance (i.e. substrate metabolism and muscle fibre type recruitment during HIIE), there was no evidence of improvement in blood redox status which has been previously associated with enhanced exercise performance after NAC supplementation. An explanation could be that the participants were well trained and therefore, RONS generated during HIIE may not have exceeded their endogenous antioxidant capacity.

Finally, the effect of postexercise NAC supplementation on redox status and inflammatory markers was examined by one study [62]. Ten young recreationally trained males participated in a double-blind, crossover design study. Participants received placebo or NAC (20 mg/kg body mass) after muscle-damaging exercise (300 eccentric contractions) for 8 days. NAC supplementation resulted in lower increases in GSSG, protein carbonyls and TBARS and lower decrease in GSH after exercise compared to placebo at various time points. Throughout recovery, GSH/GSSG ratio was higher compared to placebo. Moreover, NAC supplementation resulted in lower increases in inflammatory markers of muscle damage (as indicated by CK activity, C-reactive protein and proinflammatory cytokines), NFκB phosphorylation, and lower decrease in strength during the first two days after exercise test. However, exercise performance was completely recovered after 8 days only in the placebo group. These results indicate that NAC influences reduced oxidative damage and inflammatory response to muscle-damaging exercise and enhanced performance; however, most of these effects lasted for a short period of time, whereas exercise performance was not completely recovered 8 days after exercise compared to placebo. Therefore, supplementation with NAC or other antioxidants may delay the long-term recovery from muscle-damaging exercise by interfering with intracellular signalling pathways as previously proposed [63].

Taken together, research on the acute and short-term effects of oral NAC supplementation on redox status and exercise performance has provided inconsistent results. Although most studies have shown that NAC improves redox status at rest and also ameliorates exercise-induced oxidative stress, not all of them have associated this effect with improved exercise performance. Because exercise-induced oxidative stress in the working skeletal muscle may be essential for exercise adaptations, NAC supplementation may be an appropriate strategy to enhance exercise performance only when oxidative stress occurs (e.g. in overtrained athletes or patients with oxidative stress—associated diseases). Moreover, long-term NAC supplementation studies are lacking and unequivocally could provide useful information.

Effects of protein supplementation during exercise or training on redox status and performance

It is clear that there is a vast amount of research regarding the supplementation with exogenous

antioxidant compounds during exercise on the effects of sports performance and redox balance. Another nutritional supplement, however, that has drawn the attention of the investigators in the field is protein. Protein has been shown to increase muscle mass, promote recovery and also provide protection against exercise-induced muscle damage [64]. Of special interest is whey protein. Whey protein is the product that remains in the aqueous environment after milk curdling during cheese manufacturing. It has been considered a waste product by the dairy industry until recently when it was shown that whey protein actually contains 15–20% of total milk proteins which is a very high amount of protein to remain unused [65]. Its high content in branched-chain amino acids, L-arginine, L-lysine, L-glutamine and other amino acids, makes whey protein a high-quality, valuable nutritional supplement. Interestingly, it has been shown that whey protein also contains sulphur-containing amino acids which attenuate the reduction of intracellular glutathione concentration during stress conditions such as exercise [66]. Therefore, it has been hypothesized that whey protein supplementation in relation to exercise would provide beneficial antioxidant properties against the exercise-induced oxidative stress and subsequently improve muscle function and performance. The results from protein supplementation studies after acute and chronic exercise on redox status perturbations are given in Table 4.

The first studies that investigated the aforementioned notion implemented an acute bout of exercise. Hill et al. [67] examined the effects of both soy and whey protein before an acute bout of resistance exercise on lipid peroxidation in young males, and they reported that whey protein provided a protective effect, however, at a lower level than soy protein. The same group described similar results with regards to lipid peroxidation when the same protocol was applied to female subjects [68]. In addition, in the latter study, the group also assessed the antioxidant status and muscle damage after the exercise bout, and they found that whey protein supplementation was not adequate to increase the antioxidant capacity or to protect against muscle damage. Rankin et al. [69], a couple of years later, also failed to show any increases in the glutathione antioxidant defence system after supplementation with whey protein in cyclists before an acute bout of endurance exercise. Interestingly, Kerasioti et al. [70], in a later study in which young male individuals consumed a special cake consisting of carbohydrates and whey protein after acute cycling exercise, demonstrated that whey protein attenuated the exercise-induced lipid peroxidation. It is worth noticing that the same group published very recently an animal study [71] in which they showed that supplementation with whey protein for 28 days increased significantly the antioxidant defence mechanisms and attenuated lipid and protein oxidation in a number of tissues. Although exercise was not included in this protocol design, the results clearly indicate a beneficial effect of the whey protein in the redox status in this animal model.

A very recent study from our laboratory examined the effects of protein supplementation on performance recovery and inflammatory responses during a simulated one-week in-season microcycle with two soccer games performed three days apart [72]. The results indicate that protein feeding may be more efficient in restoring football-specific performance and strength and providing antioxidant protection during a congested game fixture.

In addition, there are a small number of studies that have looked on the effects of whey protein supplementation in relation to chronic exercise, and the results also appear equivocal. Brown et al. [73] investigated the effects of both whey and soy protein during a nine-week resistance training protocol. Although both supplements enhanced lean body mass, whey protein supplementation did not offer any antioxidant effect compared to soy protein, as revealed by decreases in the plasma antioxidant status and increases of oxidative stress markers in the whey-supplemented group. However, these results are contradicted by those of Sheikholeslami Vatani and Ahmadi Kani Golzar [74] who found that whey protein, when administered during 6 weeks of weight training in overweight individuals, improves the antioxidant defence system and some of the main metabolic parameters. Beneficial effects of whey protein during a combined aerobic and resistance training protocol were also reported in patients with chronic obstructive pulmonary disease (COPD) [75]. In the latter study, Laviolette et al. [75], although not finding any effect in antioxidant mechanisms, clearly demonstrated increases in exercise performance and quality of life of patients with COPD.

Collectively, it becomes evident that whey protein supplementation in relation to exercise can exert beneficial effects with regards to the toxicity of the redox imbalance and exercise performance. The studies available until now vary greatly in methodological aspects and participants; therefore, generalized conclusions and recommendations cannot be made currently. One could speculate that the beneficial effects of whey supplementation are more evident in patient populations than in healthy individuals; however, more mechanistic studies are required to elucidate on that notion.

Gut microbiota, oxidative stress and sport performance

Gut microbiota

Gut microbiota is the multifaceted community of microorganisms that live in the gastrointestinal tract (GI) of humans and animals. Gut microbiota contains more

Table 4 Effect of protein supplementation during endurance or resistance exercise training on performance and redox parameters.

Study	Subjects	Age	Training protocol	Nutritional supplementation protocol	Effect of training/exercise	Effect of supplementation	Effect of training/exercise	Effect of supplementation
					Performance		Redox status	
Acute exercise								
Hill at el. 2004	18 recreationally trained males	–	1 resistance exercise bout	4 weeks. Soy protein vs antioxidant-poor whey protein, 40 g/day	–	–	–	↓Lipid peroxides in soy group more than in whey protein
Box et al. 2005	18 recreationally trained females	–	1 resistance exercise bout	4 weeks. Antioxidant-rich soy protein vs antioxidant-poor whey protein, 40 g/day	–	↓CK	–	↑ preexercise antioxidant status in soy group ↓Lipid peroxides in soy group
Rankin et al. 2006	20 male cyclists	Whey protein group: 21.7 ± 0.7 yrs. Casein group: 23.4 ± 1.0 yrs	1 endurance exercise bout at day 14 and 21 of the supplementation	21 days. Whey vs casein protein 40 g/day, followed by 4 days of energy restriction	–		–	↔Total glutathione
Kerasioti et al. 2012	9 physically active males	28 ± 2 yrs.	1 endurance exercise bout (cycling)	Whey protein enriched cake: 0.9 g of carbohydrate/kg body weight/h and 0.28 g of protein/kg body weight/h. Placebo cake: 1.1 g of carbohydrate/kg body weight/h and 0.1 g of protein/kg body weight/h.	–	No effect	↑TBARS ↔Protein carbonyls ↔TAC ↔GSH ↔CAT	↓TBARS ↔Protein carbonyls ↔TAC ↔GSH ↔CAT
Poulios et al. 2018	20 football players	20.6 ± 1.1 yrs	2 × 90-min football games (3 days apart) and 4 practices/trial	SG: During game days, 80 g of milk protein concentrate; Placebo During training days, 20 g of protein	↓Locomotor activity ↓Intensity ↔Fatigue resistance ↓Muscle strength	↔Locomotor activity ↔Intensity ↑Fatigue resistance ↔Muscle strength	↔Recovery of protein and lipid peroxidation ↓GSH ↑TAC	↑Recovery of protein and lipid peroxidation ↔GSH ↑TAC
Chronic exercise								
Brown et al. 2004	27 male experienced weight lifters	19–25 yrs	9 weeks of resistance training	9 weeks. SG: 33 g of soy protein/day; Placebo: whey protein 33 g/day; Control: only training	No effect	↑Lean body mass in soy and whey protein groups	↓Plasma antioxidant status ↑Oxidative stress (myeloperoxidase)	↓Plasma antioxidant status in whey protein group ↑Oxidative stress (myeloperoxidase) in whey protein group
Sheikholeslami Vatani & Ahmadi Kani Golzar 2012	30 overweight males	23.4 ± 3.6 yrs	6 weeks of resistance training, 3 days/week	6 weeks. SG: Whey protein 90 g/day + training; Placebo: only training; Control group	↔HDL ↓Fat mass to a lower extent than protein group	↑HDL ↓Fat mass	↔TAC ↑GSH to lower extent than protein group	↑TAC ↑GSH
Laviolette et al. 2010	22 patients with COPD	SG: 62.9 ± 10.1 yrs, PL: 67.6 ± 4.4 yrs	First 8 weeks usual physical exercise and remaining 8 weeks endurance and resistance training, 3 days/week	16 weeks. SG: pressurized whey protein, 0.25 ± 0.4 g/kg/day; Placebo: casein protein, 0.30 ± 0.60 g/kg/day	–	↑Endurance in whey protein group ↑Quality of life	No effect	No effect

SG: supplemented group; CK: creatine kinase; TBARS: thiobarbituric acid reactive substances; TAC: total antioxidant capacity; GSH: reduced glutathione; CAT: catalase; HDL: high-density lipoprotein; COPD: chronic obstructive pulmonary disease.

than 100 trillion microorganisms of approximately 160 species and 9 million genes [76]. The variety of microbes colonizing the human gut is almost 10 times that of the total cells in a human, and the genetic materials are more than 150-fold that of humans [77]. Classified by phyla, the gut microbiota mainly comprises of Firmicutes and Bacteroidetes, which account for 80–90% of all gut microbes, followed by Actinobacteria and Proteobacteria. Among these phyla, *Firmicutes* mainly includes *Ruminococcus*, *Clostridium*, *Lactobacillus*, *Eubacterium*, *Faecalibacterium* and *Roseburia*, whereas Bacteroides mainly comprises *Prevotella* and *Xylanibacter* [78]. Despite the consistency of these main components, their relative proportions and the species present vary markedly across individuals [79]. Gut microbiota is influenced by several factors, including host genetics, age and some environmental factors such as diet [80], stress [79] and antibiotic intake [81].

Most gut microbes are either harmless or beneficial to the host [79]. The gut microbiota protects against enteropathogens [82,83], contributes to normal immune function [84], neutralizes drugs and carcinogens [81], synthesizes folate [85] and regulates inflammatory responses [86] and oxidative stress [87]. In addition, gut microbiota promotes the digestion and absorption of food [88], which is highly associated with energy utilization and metabolism during exercise [89,90]. In contrast, disruptions to the normal balance or dysbiosis between the gut microbiota and the host have been associated with obesity [91], malnutrition [92], inflammatory bowel disease (IBD) [93], neurological disorders [94] and cancer [95], as well as increased oxidative stress and reduced exercise performance [96]. Therefore, research in recent years has focused on understanding the impact of gut microbiota to promote overall GI health. In addition, there is an increasing interest among exercise experts and sport nutritionists regarding the effect that gut microbiota may have on exercise performance and training adaptations.

The effect of exercise on gut microbiota

Data regarding the relation between exercise and gut microbiota are limited, yet the evidence existing so-far suggests that exercise has the potential to influence gut microbiota composition in favour of health-promoting bacteria [97–101], and this is a newly introduced mechanism by which exercise may promote beneficial health effects. In addition, with being limited, most of the data regarding the effect of exercise in gut microbiota come from studies conducted in animals [102–104], and only few human studies examined the effect of exercise on gut microbiota. A common finding in animal and human studies is an increase in species richness (α-diversity) with exercise [97]. A summary of the effect of probiotics supplementation on gut microbiota and oxidative stress during exercise is given in Table 5.

Of the few human studies, only two compared the gut microbiota of athletes [98] and active premenopausal women [105] with that of healthy sedentary controls. Clarke et al. [98] reported greater α-diversity of gut microbiota in elite professional rugby players (22 phyla, 68 families and 113 genera) compared to sedentary controls (11 phyla, 33 families and 65 genera) of both high and low body mass index (BMI). To be more specific, at phyla level, rugby players had greater proportions of Firmicutes and lower proportions of Bacteroidetes than controls. At the genus level, athletes had lower overall abundances of *Bacteroides* and *Lactobacillus* and higher proportions of *Akkermansia muciniphila*, a mucin-degrading microbe positively correlated with improved metabolic profile [106,107]. However, the extreme dietary differences between the rugby players and sedentary individuals of that study cannot be ignored, and it is unclear if this effect was due to exercise, a high-protein diet or a combination of the two factors as diet has been shown to affect gut microbiota composition [80]. In a more recent study [105], higher abundance of the health-promoting bacteria *Akkermansia* along with *Bifidobacterium*, *Faecalibacterium* and *Roseburia* in active than in sedentary premenopausal women has been reported. Although the species richness was similar between the two groups, an inverse association between sedentary parameters and microbiota richness existed. The different outcome regarding species richness in the aforementioned two studies may be due to the different training workload and total demands between professional athletes and physically active individuals. It seems that a specific amount of total workload is required to efficiently induce changes in the diversity of gut microbiota, yet the current limited data do not allow for any valid conclusions to be made, and further research is need.

Although no direct comparison was applied between athletes or physically active and sedentary participants, a few more recent studies have also found greater species richness [99] and higher abundances of health-promoting bacteria [108] in individuals with higher cardiorespiratory fitness than in less fit and less active individuals. Estaki et al. [99] found that cardiorespiratory fitness (expressed via VO_{2peak}) of healthy young adults significantly contributed to increased α-diversity; in fact, VO_{2peak} alone accounted for more than 20% of the variation in taxonomic richness, outperforming several other variables including sex, age, BMI and dietary components. An interesting finding in that study was that high cardiorespiratory fitness also correlated with an increase in the short-chain fatty acid (SCFA) butyrate, a microbial metabolite that exerts anticarcinogenic and antiinflammatory properties and, along with propionate and acetate, provides 10% of the daily caloric requirements in humans [109]. The increases in fecal butyrate were concomitant with increased relative abundances of butyrate-producing

Table 5 Effects of probiotics supplementation on gut microbiota and oxidative stress during exercise.

Study	Subjects	Age	Training protocol	Nutritional supplementation protocol	Effect of training/exercise	Effect of supplementation
					Redox status/inflammation	
Acute exercise						
Lamprecht et al. 2012	23 endurance-trained men	Probiotics group: 37.6 ± 4.7 yrs. Placebo: 38.2 ± 4.4 yrs.	90-min intense cycle ergometry	14 weeks of multispecies probiotics (1010 CFU/day, Ecologic® Performance or OMNi-BiOTiC® POWER	↑PC ↔MDA ↔TOS ↔TNF-α ↑IL-6	↓Zonulin at rest ↔α1-antitrypsin at rest ↔PC ↔MDA ↔TOS ↔TNF-α ↔ IL-6
Chronic exercise						
Martarelli et al. 2011	24 amateur male cyclists (control: *n* = 12, probiotic group: *n* = 12)	32.03 ± 6.12 yrs.	4 weeks of intense training season	4 weeks of probiotic strains (1:1 *Lactobacillus. rhamnosus* IMC 501® and *L. paracasei* IMC 502®; 109 cells/day)	↑ROMs in the control group ↔BAP in the control group	↔ ROMs in the probiotic group ↑BAP in the probiotic group
Valimaki et al. 2012	119 recreational runners (placebo: *n* = 58), probiotics, *n* = 61)	22–69 yrs.	90 days of training (T2) + 6 days (T3) preparation for the Helsinki marathon race (T4)	4 weeks of *Lactobacillus rhamnosus* GG (2 capsules of 5.0 × 109 CFU/day) or placebo	Ox-LDL: ↑by 28% from T2 to T3, ↓by 16% from T3 to T4 in the placebo group S-TRAP level: ↑by 16% from T3 to T4 in the placebo group S-γ-tocopherol: ↓by 38% during the training period, ↑by 54% from T2 to T4 S-α-tocopherol: ↓by 14% from T2 to T3 in the placebo group S-β-carotene: ↔from T1 to T2 and from T3 to T4 and ↓by 42% from T2 to T3 in the placebo group S-ubiquinone-10: ↑by 29% from T3 to T4 and ↓by 18% from T2 to T3 in the placebo group	Ox-LDL: ↑by 33% from T2 to T3, ↓by 19% from T3 to T4 in the probiotics group S-TRAP level: ↑by 16% from T3 to T4 in the probiotics group S-γ-tocopherol: ↓by 38% during the training period S-α-tocopherol: ↓by 11% from T2 to T3 in the probiotics group S-β-carotene: ↔from T1 to T2 and from T3 to T4 in the probiotics group and ↓by 43% from T2 to T3 in the probiotics group S-ubiquinone-10: ↑by 18% from T3 to T4, ↑by 23% from T2 to T3 and ↓by 26% from T2 to T3 in the probiotics group
Gleeson et al. 2011	58 endurance-trained individuals (placebo: *n* = 26, probiotic group: *n* = 32)	Placebo group: 25 ± 9 yrs., probiotics group: 32 ± 14 yrs.	Usual training program	16 weeks of 6.5 × 109 live cells of *L. casei* Shirota twice a day	Whole-blood cultures 8 & 16 weeks: ↓IL-2, ↓IL4, ↓IL-6, ↓IL-8, ↓TNF-α 16 weeks: ↓IL-1β, ↓IFN-γ, ↓MPC-1	↓in URTI symptoms and URTI episodes ↑saliva IgA ↔plasma IgA, IgG, IgM and total Ig

MDA: malondialdehyde; TOS: total oxidation status of lipids; TNF-α: tumour necrosis factor-alpha; IL-6: interleukin-6; IL-2: interleukin-2; IL-4: interleukin-4; IL-8: interleukin-8; ROMs: reactive oxygen metabolites; BAP: biological antioxidant potential; Ox-LDL: oxidized low-density lipoprotein; S-TRAP: antioxidant potential of serum; S-γ-tocopherol: serum γ-tocopherol; S-α-tocopherol: serum α-tocopherol; S-β-carotene: serum β-carotene; IFN-γ: interferon-γ; MPC-1: macrophage chemoattractant protein-1; URTI: upper respiratory tract infection; IgA: immunoglobulin A; IgG: immunoglobulin G; IgM: immunoglobulin M; CFU: colony-forming unit.

taxa such as Clostridiales, *Roseburia*, Lachnospiraceae and Erysipelotrichaceae [99]. In another study [108], the authors examined the composition of the gut microbiota in endurance athletes (cyclists). The microbiome of 33 cyclists was split into three taxonomic clusters, characterized by high *Prevotella*, high *Bacteroides* or a mix of many genera including *Bacteroides*, *Prevotella*, *Eubacterium*, *Ruminococcus* and *Akkermansia*. In addition, the high relative abundance of the genus *Prevotella* ($\geq$2.5%) positively correlated with the time spent for exercise training during an average week. Furthermore, the increased abundance of *Prevotella* correlated with amino acid (AA) and carbohydrate metabolism pathways, including branched-chain amino acids (BCAA), and these pathways have been shown to decrease exercise-induced muscle fatigue, promote muscle protein synthesis [110] and attenuate muscle damage during prolonged endurance exercise [111]. These results suggest that a gut microbiota containing *Prevotella* to synthesize or influence other microbes to produce BCAAs would be of great benefit in the recovery of athletes from intense exercise.

The beneficial effects of exercise training on gut microbiota seem to depend on the sustainment of exercise and are largely reversed once exercise training is ceased. Six weeks of endurance exercise training altered the gut microbiota and microbium-derived SCFAs in previously sedentary individuals [112]. As in the study by Estaki et al. [99], in the study of Allen et al. [112], the exercise-induced increases in butyrate concentrations were associated with increases in butyrate-producing taxa of *Faecalibacterium*, *Roseburia*, *Lachnospira*, Lachnospiraceae and Clostridiales. However, the positive alterations of gut microbiome in response to exercise training were reversed after 6 weeks of training cessation. This finding provides further evidence that physical activity status contributes significantly to the composition of the human gut microbiota.

Not only chronic but also acute strenuous exercise seems to cause changes in the composition of gut microbiota. Karl et al. [100] demonstrated that demanding military training exercise provokes alterations in intestinal microbiota composition and metabolism, which are accompanied by increased intestinal permeability. What was interesting in that study was the fact that changes in microbiota composition were broadly characterized by the increase in abundance of less dominant and potentially deleterious and infectious taxa (e.g. *Peptostreptococcus* and *Staphylococcus*) at the expense of a more dominant taxa that is thought to protect against pathogen invasion, reduce inflammation and promote immunity (e.g. *Bacteroide*s and *Faecalibacterium*). The unexpected change in the ratio of less-abundant, potentially harmful taxa to beneficial taxa may account for the accompanied increase in intestinal permeability, although the larger increases in Shannon diversity during military exercise were observed in individuals with the lowest preexercise diversity. Therefore, finding ways to increase GI health—promoting bacteria before exercise may provoke the increase in abundance of potentially deleterious and infectious taxa and avoid the disturbance of gut permeability during exercise. However, the results of that study must also be interpreted with caution as the demanding physiological stress was also coupled by extreme dietary differences.

Considering the acute strenuous exercise effects mentioned in the previous paragraph, exercise could positively influence the human gut microbiota composition by increasing diversity and favouring the increase of relative abundances of health-promoting microbial species. Gut microbiota is related with several factors such as the type and amount of exercise, diet, host immunity and host metabolism. Further studies are warranted for understanding the impact of these factors on the metabolic function of the gut microbiome and how organisms such as *Akkermansia*, *Prevotella*, *Faecalibacterium*, *Roseburia*, *Lachnospira*, Lachnospiraceae and Clostridiales may respond to exercise and, in turn, positively influence health and athletic performance.

Gut microbiota and oxidative stress during exercise

Research connecting the relationship between gut microbiota and GI redox status during exercise is just at the beginning. However, the emerging evidence points towards a relationship between gut microbiota, exercise and redox status in the GI tract in humans and animals [101].

The GI tract is a key source of RONS, and redox homeostasis is regulated through enzymatic (e.g. SOD, catalase [CAT] and GPx) and nonenzymatic mechanisms (e.g. urate, glutathione, ubiquinone, thioredoxin, ferritin and lactoferrin) [113]. Redox homeostasis in the GI tract is crucial for nutrient digestion and absorption, stem cell proliferation, apical enterocyte apoptosis and immune response [114], whereas oxidative stress is related to the pathogenesis of various GI diseases such as peptic ulcers, cancers and IBD [113]. Specific gut microbiota composition seems to predispose to a balanced redox environment. Xu et al. [87] demonstrated that *Lactobacillus* and *Bifidobacterium* in the jejunum and colon of early weaned piglets exhibited a positive correlation with total antioxidant capacity (T-AOC), SOD, glutathione peroxidase (GSH-Px) and inhibition capacity of hydroxyl radical (IHR) and a negative correlation with MDA and hydrogen peroxide (H_2O_2). On the other hand, *Escherichia coli* presented negative correlation with T-AOC, SOD, GSH-Px and IHR and positive correlation with MDA and H_2O_2.

Given the modulating effects of gut microbiota on antioxidant enzyme activity and the ability of antioxidant

enzymes to augment recovery after extreme exercise or high-volume training, Hsu at al. [96] examined the effect of gut microbiota status on various antioxidant levels and exercise performance in specific pathogen-free (SPF), germ-free (GF) and *Bacteroides fragilis* (BF) gnotobiotic mice after exhaustive exercise. The absence of microbiota (GF conditions) decreased antioxidant enzyme activities after exercise as evidenced by the lower serum and hepatic GPx activity in GF compared with SPF and BF mice and the higher serum CAT activity in SPF compared with GF and BF mice. The down-regulation of GPx and CAT was accompanied by a decreased time-performance. These findings suggest that loss of microbes might be associated with down-regulated activity of antioxidants, but existing microbes (SPF and BF mice) may enhance antioxidant enzymes' activity to ameliorate exercise-induced fatigue and probably increase exercise performance. Further research is needed to shed light on the role of gut microbiota on modulating redox responses and subsequently affecting exercise-induced fatigue and performance.

The effect of probiotics supplementation on gut microbiota, oxidative stress and exercise performance

Considering the role that gut microbiota may play in modulating redox responses during exercise, one could speculate that manipulating gut microbiota towards increased abundances of species that promote the upregulation of antioxidants would be of great importance for confronting the toxic effects of oxidative stress during exercise and probably enhancing performance.

Probiotic supplementation is attracting attention of sports experts and dieticians as a means to improve GI microbiota ecosystems and promote athletes' good health and exercise performance [115–117]. Probiotics are food supplements that contain live microorganisms, especially lactic acid bacteria, which when administered in adequate amounts confer a health benefit for the host [118]. They are available as tablets, capsules, powder, and probiotic-enriched chews or in selected dairy products such as fermented milk or yogurt [117]. Few studies have explored the antioxidant properties of probiotics, indicating that some probiotic strains positively influence and correct oxidative stress in humans, through their direct antioxidant activity, improvement of food digestion and absorption, vitamin production and immune system modulation [116,119–121].

Studies conducted on athletes indicate that probiotics have clinical benefits in terms of reduced frequency, severity and/or duration of respiratory and gastrointestinal illness [117,118]. Furthermore, limited data support the notion that probiotics may counteract exercise-induced oxidative stress. Martarelli et al. [116] examined the effect of *Lactobacillus rhamnosus* and *Lactobacillus paracasei* supplementation during a 4-week period of intense training on exercise-induced oxidative stress. The authors reported decreased oxidative stress and increased plasma antioxidant levels in athletes under the probiotics supplementation condition. More specifically, in vitro analysis showed that *L. rhamnosus* IMC 501® and *L. paracasei* IMC 502® (109 cells/day) recovered from human faeces after probiotic supplementation had an antioxidative effect on inhibiting lipid peroxidation. In addition, the in vivo data revealed that probiotics supplementation decreased plasma levels of reactive oxygen metabolites (ROMs), consistently with an increase in plasma antioxidants levels, whereas in the control group, the ROM levels after 4 weeks of intense exercise were higher than those measured before exercise.

In another study, Lamprecht et al. [115] investigated the effects of 14 weeks of probiotic supplementation (1010 CFU/day, Ecologic® Performance or OMNi-BiOTiC® POWER) on markers of intestinal barrier, oxidation and inflammation in rest and after intense exercise in trained men. Zonulin (a marker of intestinal barrier integrity) and also protein carbonyls (PCs) and total lipid peroxides (TOS), as well as TNF-α, were already above normal at baseline, indicating that these trained men may have suffered oxidative stress and a low-grade inflammation due to compromised intestinal barrier function, which was likely evoked by chronic exercise stress. Probiotics supplementation recovered the increased concentration of zonulin. In contrast with the study of Martarelli et al. [116], probiotics did not manage to provoke any significant changes in both at rest and after intense exercise on PC, MDA, TOS, TNF-α or interleukin (IL)-6, although there was a trend for lower PC and TNF-α in the supplemented than in the control group. Similarly, *Lactobacillus rhamnosus* supplementation in the form of milk-based fruit drink (ATCC 53103 bacteria, 3.0 × 108 colony-forming unit/ml) or capsules (5.0 × 109 colony-forming unit/capsule) for three months did not alter oxidized LDL levels, the antioxidant potential of serum (TRAP) or vitamins compared with the placebo group during the training period, the 6-days preparative period before, and after a marathon run [122].

Obviously, the current limited data do not allow for valid conclusions regarding the effectiveness of the probiotics supplementation to beneficially influence exercise-related changes of redox status, and more research is warranted. This would be of great importance not only for athletic performance but also for boosting the overall exercise-modulated and redox-related GI health.

Conclusion

This review summarized the existing evidence regarding the use of conventional supplements with antioxidant properties on exercise-induced oxidative

stress and athletic performance. Supplementation with the most widely used vitamins, that is, vitamin C and E, has produced mixed results because in some cases, it might lead to unwanted results such as decreased exercise performance and training adaptations. Supplementation with the most widely used polyphenols that have been used as supplements in relation to exercise-induced oxidative stress, that is, resveratrol and catechins, has also produced mixed results with some studies indicating beneficial effects on redox perturbations after an acute bout of exercise and also after a longer supplementation period. Even though NAC supplementation seems to confer a protection by ameliorating the exercise-induced oxidative stress, it does not look like these results coincide with better exercise performance. Protein ingestion seems to be promising not only by scaling down the redox status perturbations after exercise but also by leading to better exercise performance. How these two are related is something that needs to be determined in future studies. Finally, because exercise leads to a blood flow redistribution during exercise and seems to affect the gut microbiota, an attempt was made to review the few studies that assessed the relationship between exercise and gut microbiota responses. It seems that exercise could positively influence the human gut microbiota composition by increasing diversity and favouring the increase of relative abundances of health-promoting microbial species. However, the contribution of several factors such as the type and amount of exercise, diet, host metabolism and immunity on metabolic function and exercise performance needs to be determined in future studies. At the moment, it is not clear whether a definite recommendation in favour or avoidance of the reviewed supplements could be made. Supplementation in athletes with deficiencies and in greater need, such as overtraining, is definitely something that needs to be determined in future studies.

Conflict of interest statement

Nothing declared.

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