Lamprecht M, editor. Antioxidants in Sport Nutrition. Boca Raton (FL): CRC Press/Taylor & Francis; 2015.

Chapter 3 Antioxidants in Athlete's Basic Nutrition

Considerations towards a Guideline for the Intake of Vitamin C and Vitamin E

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3.1. INTRODUCTION: ANTIOXIDANTS—A REMAINING HOT TOPIC IN SPORT NUTRITION

Antioxidants in acute physical exercise and exercise training remain a hot topic in sport nutrition, exercise physiology and biology, in general (Jackson, 2008; Margaritis and Rousseau, 2008; Gomez-Cabrera et al., 2012; Nikolaidis et al., 2012). During the past few decades, antioxidants have received attention predominantly as a nutritional strategy for preventing or minimising detrimental effects of reactive oxygen and nitrogen species (RONS), which are generated during and after strenuous exercise (Jackson, 2008, 2009; Powers and Jackson, 2008). Antioxidant supplementation has become a common practice among athletes as a means to (theoretically) reduce oxidative stress, promote recovery and enhance performance (Peternelj and Coombes, 2011). However, until now, requirements of antioxidant micronutrients and antioxidant compounds for athletes training for and competing in different sport events, including marathon running, triathlon races or team sport events involving repeated sprinting, have not been determined sufficiently (Williams et al., 2006; Margaritis and Rousseau, 2008). Crucially, evidence has been emerging that higher dosages of antioxidants may not necessarily be beneficial in this context, but can also elicit detrimental effects by interfering with performance-enhancing (Gomez-Cabrera et al., 2008) and health-promoting training adaptations (Ristow et al., 2009). As originally postulated in a pioneering study on exercise-induced production of RONS by Davies et al. (1982) in the early 1980s, evidence has been increasing in recent years that RONS are not only damaging agents, but also act as signalling molecules for regulating muscle function (Reid, 2001; Jackson, 2008) and for initiating adaptive responses to exercise (Jackson, 2009; Powers et al., 2010). The recognition that antioxidants could, vice versa, interact with the signalling pathways underlying the responses to acute (and repeated) bouts of exercise has contributed important novel aspects to the continued discussion on antioxidant requirements for athletes.

In view of the recent advances in this field, it is the aim of this report to examine the current knowledge of antioxidants, in particular of vitamins C and E, in the basic nutrition of athletes. While overviews on related topics including basic mechanisms of exercise-induced oxidative stress, redox biology, antioxidant defence systems and a summary of studies on antioxidant supplementation during exercise training are provided, this does not mean that this report is comprehensive. Several issues of the expanding and multidisciplinary field of antioxidants and exercise are covered elsewhere in this book and/or in the literature. Exemplarily, the reader is referred to reviews on oxidative stress (König et al., 2001; Vollaard et al., 2005; Knez et al., 2006; Powers and Jackson, 2008; Nikolaidis et al., 2012), redox-sensitive signalling and muscle function (Reid, 2001; Vollaard et al., 2005; Jackson, 2008; Ji, 2008; Powers and Jackson, 2008; Powers et al., 2010; Radak et al., 2013) and antioxidant supplementation (Williams et al., 2006; Peake et al., 2007; Peternelj and Coombes, 2011) in the context with exercise. Within the scope of the report, we rather aim to address the question regarding requirements of antioxidants, specifically vitamins C and E, during exercise training, draw conclusions and provide practical implications from the recent research.

3.2. OVERVIEW ON BASIC MECHANISMS OF EXERCISE-INDUCED OXIDATIVE STRESS

After more than three decades of research, it is well documented that prolonged, intense exercise and/or exercise involving frequent eccentric/lengthening contractions, especially if unaccustomed, induces the generation of RONS including free radicals [e.g. superoxide ($O_2^{\bullet -}$), nitric oxide ($NO^{\bullet}$), hydroxyl radical ($OH^{\bullet}$)] and non-radicals [e.g. hydrogen peroxide (H_2O_2), hypochlorous acid (HOCl)] (Vollaard et al., 2005; Jackson, 2008, 2009; Powers and Jackson, 2008). Potential mechanisms for an exercise-induced RONS generation include the activation of nicotinamide adenine dinucleotide phosphate–oxidase complexes associated with the sarcoplasmic reticulum and plasma membranes, and variations in perfusion triggering xanthine oxidase activity (Vollaard et al., 2005; Jackson, 2008; Powers and Jackson, 2008). Furthermore, an inadequate electron transfer through the mitochondrial respiratory chain related to the increased oxygen consumption has previously been assumed as a major site for an increased superoxide generation *during* muscle contractions (e.g. reviewed by Powers and Jackson, 2008). However, more recent studies indicate that the RONS generation through an increased mitochondrial oxygen flux during aerobic exercise is rather limited due to internal control mechanisms (Vollaard et al., 2005; Jackson, 2008; Powers and Jackson, 2008). In addition, muscular inflammatory responses characterised by an infiltration of neutrophils and macrophages into exercised skeletal muscle (Stupka et al., 2000), followed by oxidative burst reactions, could contribute to an increased RONS generation until a few days *after* exercise involving muscle damage (Close et al., 2003). Although the phagocytic activity of infiltrated leukocytes appears to be essential for the repair and regeneration of injured muscle tissue, the free-radical-mediated removal of cell debris by phagocytic cells such as neutrophils may elicit secondary tissue damage (Close et al., 2003; Tidball and Villalta, 2010). Each of these potential mechanisms occurs in skeletal muscle tissue, which, as one of the biggest tissues in the human body, is therefore considered the major source for the generation of ROS related to exercise (Powers and Jackson, 2008). However, other tissues have also been discussed as potential sources for an increased exercise-induced RONS generation, including the heart, lungs (Powers and Jackson, 2008) and blood constituents such as leukocytes (Nikolaidis and Jamurtas, 2009), which are mobilised into the circulation and activated as part of the systemic inflammatory response to intense, prolonged exercise (König et al., 2001; Neubauer et al., 2008b, 2013).

Owing to their reactivity, RONS can oxidise and alter the structure and/or function of biomolecules, among which lipids, proteins and DNA

are the most vulnerable (and most investigated) cellular targets (Halliwell and Gutteridge, 2007). Depending on the type of stress imposed and how severe the stress is, RONS may accumulate, eventually leading to oxidative damage to these macromolecules and subsequently to an impairment of their physiological functions (Halliwell and Gutteridge, 2007). Progressive oxidative macromolecular damage is evidenced, for example, by disruptions in the cell membrane lipid bilayer, inactivation of membrane-bound proteins, loss of enzyme function, lipoprotein peroxidation and DNA strand breakage (Halliwell and Gutteridge, 2007). Furthermore, it is now recognised that oxidative stress may occur without necessarily resulting in an overall imbalance between pro-oxidants and antioxidants, but rather through a disruption of individual redox-sensitive signalling pathways, some of which, for example, promote proteolytic degradation, inflammation and cell death (Jones, 2006; Jackson, 2009; Powers et al., 2010; Nikolaidis et al., 2012). The chronic exposure to high levels of RONS is associated with the development and/or progression of pathophysiological processes, and implicated in an increasing number of human diseases, such as cardiovascular, metabolic, inflammatory and neurogenerative diseases, cancer as well as muscle atrophy and the ageing process (Vollaard et al., 2005; Halliwell and Gutteridge, 2007; Powers et al., 2010). Exercise-induced oxidative stress has been discussed to impair performance and muscle force production during exercise (Reid, 2001; Vollaard et al., 2005; Powers and Jackson, 2008), contribute to muscle damage and further promote inflammatory responses after exercise, thereby interfering with recovery (König et al., 2001). Indications for increased oxidative stress have also been reported during periods of overtraining (Palazzetti et al., 2004). Furthermore, some empirical and epidemiological data, paradoxically, suggest that an extraordinary high volume of exercise is associated with an increased risk of developing cardiovascular disease (Lee et al., 1995), potentially due to cumulative oxidative stress as one of the main mechanisms (Knez et al., 2006). On the basis of these data (Lee et al., 1995) and the model of oxidative modifications in atherosclerosis (Stocker and Keaney, 2004), Knez and co-workers hypothesised that the population of ultra-endurance athletes, training for and competing in races with durations of several hours, might be at higher risk of developing atherosclerotic lesions (Knez et al., 2006). To address this issue, one of us together with co-workers recently investigated the time-course of recovery of a broader spectrum of lipid peroxidation and protein oxidation biomarkers in the blood plasma, as well as indices for oxidatively damaged DNA in circulating lymphocytes in response to an Ironman triathlon until 19 days post-race (Neubauer et al., 2008a, 2008c, 2010; Reichhold et al., 2008, 2009). This study indicated that despite a temporary increase in most oxidative stress markers, there is no persistent oxidative stress in response to an acute bout of ultra-endurance exercise, potentially due to training- and exercise-induced changes in the antioxidant defence system (Neubauer et al., 2008a, 2010). Furthermore, recent data of a cross-sectional study showed that physically active, former top-level athletes (who previously participated in endurance sport events and sport games) were characterised by a significantly lower cardiovascular risk profile including a lower oxidative stress status compared with sedentary, former athletes and age-matched, non-athletic individuals (Pihl et al., 2003). Taken together, so far, there is no conclusive evidence that exercise-induced oxidative stress, even in ultra-endurance athletes, elicits any negative impact on health.

3.3. OVERVIEW ON ANTIOXIDANT DEFENCE SYSTEMS, AND THE ROLE OF RONS AS SIGNALLING MOLECULES FOR ENDOGENOUS ANTIOXIDANT DEFENCES

There are several cellular antioxidant defence strategies to counterbalance RONS. These strategies include converting RONS into less active species and preventing the transformation of these less active molecules into ones with higher activity, scavenging RONS and minimising the availability of pro-oxidants (e.g. iron) (Halliwell and Gutteridge, 2007; Powers and Jackson, 2008). The composition of antioxidant defences differs from tissue to tissue and from cell-type to cell-type, but broadly, antioxidant defence systems can be classified into endogenous enzymatic and non-enzymatic antioxidants on the one side, and exogenous, that is, dietary antioxidants on the other (Halliwell and Gutteridge, 2007; Powers and Jackson, 2008). The enzymatic antioxidant defence consists of primary antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT), and accessory antioxidant enzymes such as thioredoxin (Halliwell and Gutteridge, 2007; Powers and Jackson, 2008). Examples for non-enzymatic endogenously produced low-molecular weight antioxidants are glutathione, uric acid and bilirubin (Halliwell and Gutteridge, 2007; Powers and Jackson, 2008). Despite some controversial results (e.g. reviewed by Powers and Jackson, 2008), most studies investigating the adaptive responses to exercise-induced RONS generation have shown that both acute (Khassaf et al., 2001, 2003) and regular exercise (Brooks et al., 2008) induces increased activities of antioxidant defence enzymes, in particular SOD, in skeletal muscle (Khassaf et al., 2001, 2003) in mice (McArdle et al., 2004; Brooks et al., 2008) and humans (Khassaf et al., 2001, 2003). The increased SOD activity in the muscle of mice reported in a study of Malcolm Jackson's research group (Brooks et al., 2008) appeared to be primarily due to an increased SOD protein content, reflecting a longer term adaptation to endurance exercise training to counterbalance subsequent redox disturbances and reduce the risk of oxidative damage (Powers and Jackson, 2008). Plasma concentrations of low-molecular mass antioxidants originating from endogenous sources, including bilirubin (Neubauer et al., 2010) and uric acid (Liu et al., 1999; Mastaloudis et al., 2004a; Neubauer et al., 2010), have also been reported to temporarily increase acute bouts after strenuous exercise due to various mechanisms induced during intense exercise (e.g. increased haemolysis and increased purine metabolism) (Liu et al., 1999; Neubauer et al., 2010). Although the exercise-induced changes in these endogenous low-molecular mass antioxidants might not be considered as specific training adaptations, they contribute to enhanced plasma antioxidant defences and, potentially, play a protective role against oxidative damage of blood cell components such as lymphocyte DNA (Neubauer et al., 2010).

Importantly, antioxidant defence systems work in a highly efficient and coordinated manner and are closely related to nutrition. Important low-molecular mass nutritive antioxidants include vitamin C, vitamin E (comprising tocopherols and tocotrienols), carotenoids (e.g. β-carotene) and polyphenols (e.g. flavonoids) (Halliwell and Gutteridge, 2007). Exemplarily, among numerous interactions between antioxidants, the tocopheroxyl radical, which results from the reaction of α-tocopherol with peroxyl radicals, can be 'recycled' to its active vitamin E form by other antioxidants such as vitamin C or glutathione (Traber, 2007). Furthermore, several antioxidant enzymes require

trace elements as co-factors for their structural integrity and their functionality. Trace elements with antioxidant function include selenium (required for GPX), iron (CAT), zinc, copper and manganese (all of which are required for different isoforms of SOD). For background information on the biochemistry of these nutritive antioxidants, the reader is referred to the literature (Halliwell and Gutteridge, 2007; Powers and Jackson, 2008). Within the frame of this chapter, the focus is on the vitamins C and E in the context with exercise training, as discussed below.

Of utmost importance for the continued discussion on antioxidants in sport nutrition, it has become an emerging concept that moderate levels of RONS play an important role in the regulation of the muscular contractile function and physiological adaptive responses (Jackson, 2008; Powers and Jackson, 2008; Powers et al., 2010). An increasing number of investigations indicate that RONS generated in response to physiological stimuli such as exercise are a necessary signal to activate redox-sensitive cellular pathways and transcription factors including nuclear factor-κB, activator protein-1 (AP-1), peroxisome proliferator-activated receptor transcription factors and heat-shock factor (HSF)-1 (Brooks et al., 2008; Jackson, 2008; Radak et al., 2013). In turn, these transcription factors regulate the expression of genes including genes encoding for specific stress and heat shock proteins (HSPs) (Khassaf et al., 2003), genes involved in antioxidant protection (Khassaf et al., 2003; Brooks et al., 2008) and genes associated with mitochondrial biogenesis (Irrcher et al., 2009). The up-regulation of the expression of protective genes/proteins such as HSPs and antioxidant enzymes in response to exercise-induced oxidative stress is associated with an increased protection against subsequent exposure to RONS (McArdle et al., 2004). These seemingly contradictory effects of RONS have been described by implementing the concept of hormesis into this context, a dose–response relationship in which a low dose of a substance is stimulatory or beneficial and a high dose is inhibitory or toxic (Ji et al., 2006; Radak et al., 2013).

3.4. OVERVIEW ON STUDIES ON ANTIOXIDANT SUPPLEMENTATION IN EXERCISE TRAINING

In the following section, we will provide an overview on human studies in this area. The main focus of this overview will be on chronic supplementation (i.e. more than 2 weeks) with vitamins C and E (mainly the α-tocopherol form), either individually or in combination, during exercise training, since these antioxidant vitamins were the most commonly used and more widely examined supplements in these studies. A summary of the studies included in this review is presented in Table 3.1. As mentioned, we do not claim that the list of studies included in the current report is complete, and would like to refer the reader to comprehensive reviews which are already available in this area (Vollaard et al., 2005; Williams et al., 2006; Peake et al., 2007), including a review article of Peternelj and Coombes as one of the most recent (Peternelj and Coombes, 2011). Our approach is rather to exemplarily discuss the findings of a number of key studies and their implications for defining guidelines on the antioxidant intake in athletes. Since it has been suggested that oxidative stress is relative to exercise intensity (Lamprecht et al., 2008), and that in sport with higher oxygen consumption demands, such as marathon- and triathlon-training, higher amounts of RONS are produced, the studies presented are focused on endurance athletes and/or well-trained individuals.

Early studies from the 1970s and 1980s were focused more on the effect of antioxidant supplementation on exercise performance. The rationale behind this effort was based on the fact that the RONS produced during exercise cause muscle damage and fatigue, and consequently decrease performance. It was hypothesised that supplementation with antioxidants would prevent damage or accelerate recovery and, as a result, improve exercise performance. However, the majority of these early studies did not succeed in demonstrating a significant effect of antioxidant supplementation during training. One of the first studies published in JAMA in 1970 (Gey et al., 1970) showed that daily supplementation of 1.000 mg vitamin C during training did not have any effect on endurance performance in well-trained individuals. Some years later, long-term supplementation with vitamin E (α-tocopherol) by competitive swimmers did not show any effect regarding endurance and cardiorespiratory efficiency (Lawrence et al., 1975; Sharman et al., 1976).

Later studies were focused not only on performance, but also on blood markers and redox status. Rokitzki et al. (1994) reported that administration of combined vitamins C and E for 1 month prior to a marathon race decreased indices of muscle damage after the race while there was no effect on lipid peroxidation. Furthermore, the same combination in soccer players prevented both muscle damage and lipid peroxidation, but it did not affect performance (Zoppi et al., 2006). Mastaloudis et al. (2004a) also tested the effect of the combination of vitamins C and E on lipid peroxidation and inflammation after a 50-km ultra-marathon race. The supplementation prevented lipid peroxidation in response to the ultra-marathon; however, it showed no effect on markers on inflammation which increased dramatically after exercise. One of the authors and co-workers (Yfanti et al., 2010) performed a training study where well-trained individuals consumed the same combination of antioxidant vitamins during 3 months of high-intensity cycling exercise. However, no effect on either cardiovascular or skeletal muscle aerobic adaptations was observed (Yfanti et al., 2010). In contrast, in the same study, higher levels of plasma protein oxidation and lipid peroxidation were measured in the group that consumed the antioxidants compared with placebo, suggesting a pro-oxidative effect of the vitamins (Yfanti et al., 2012). The latter study was not the first one to show such an effect. Some years earlier, Nieman et al. (2004) had found that vitamin E supplementation for 2 months before an Ironman triathlon race promoted lipid peroxidation, assessed by plasma F2-isoprostanes, and inflammation in response to acute ultra-endurance exercise. Furthermore, Knez et al. (2007) examined oxidative stress in half and full Ironman triathletes. They demonstrated that the athletes who were supplemented with vitamins C and E for ca. 1 year had higher levels of lipid peroxidation (assessed by malondialdehyde) after a half-distance- or full-Ironman race, suggesting also a pro-oxidative effect of the supplemented antioxidative vitamins. In addition, in a study by Lamprecht et al. (2009) supplementation for 2 weeks with a vitamin mixture, including vitamin C, vitamin E, β-carotene and selenium, increased plasma malondialdehyde concentration at rest.

However, even after many years of research, it is not possible to draw clear conclusions as a number of studies have not been able to clearly demonstrate excessive damaging effects of exercise with or without antioxidant supplementation. In a large-scale study in Ironman

triathletes performed by one of the authors and co-workers, it has been shown that after an ultra-endurance event, DNA-, protein- and lipid peroxidation damage might occur, but that these effects last only transiently (Neubauer et al., 2008a,c; Reichhold et al., 2008, 2009). It is worth noting that the participants in this study were consuming physiological amounts of antioxidants during the course of the study (as described in detail below) (Neubauer et al., 2010). Mastaloudis et al. (2004b) found similar results in runners after an ultra-marathon race, although the study participants were consuming high doses of vitamins C and E. Therefore, taking into account the above published research, it is difficult to support the hypothesis that antioxidant supplementation with vitamins C and E during training is necessary for athletes of ultra-endurance sport, as it seems that it offers minimal or no beneficial effect.

The subject of antioxidant supplementation and exercise training continued to be of high interest. However, the initial view that RONS were, in general, harmful and that preventing their actions would be beneficial changed over the years. This happened due to some studies showing that RONS produced during exercise play a fundamental role in cellular processes (Irrcher et al., 2009) and that blocking their action would prevent essential cellular processes from taking place.

The more recent human studies investigating the interrelation of antioxidant supplementation and exercise training implemented more sophisticated design, methodologies and techniques and were focused not only on performance, but also on the health aspects of endurance training. Khassaf et al. (2003) examined the effect of vitamin C supplementation during training on antioxidant defence mechanisms and more specifically on SOD and CAT activity, as well as on HSP60 and HSP70. They found that supplementation attenuates the adaptive response to exercise, suggesting a possible negative effect of the supplementation during training. In line with these findings, some years later Fischer et al. (2006) showed that supplementation with vitamins C and E (specifically the γ-tocopherol isoform) inhibits the exercise-induced increase of HSP72 in skeletal muscle as well as in the circulation. The above studies were performed in well-trained individuals and the doses of antioxidants consumed were 5–17 times higher than the recommended dietary allowance (RDA). It is noteworthy that when doses of vitamins C and E close to 100% of the RDA were used during intense training in competitive triathletes, endogenous antioxidant defences were preserved after a duathlon race (Palazzetti et al., 2004). These data suggest that antioxidative requirements of well-trained endurance athletes can be covered by dosages equivalent or close to the RDA, which can be provided by a balanced diet. In addition, it can be suggested that extremely high dosages of antioxidant vitamins that are usually consumed by athletes and individuals engaged to habitual exercise do not offer any additional beneficial effect, but in contrast, they appear in many cases to be harmful.

A number of studies have been published lately which focused on health-related adaptations to endurance training and how antioxidant supplementation interferes in these processes. Although these studies were not performed in well-trained individuals, we believe it is worth mentioning them here as they were the studies that changed the view in the sport world that antioxidant supplements might after all not be required during training. In a study by Gomez-Cabrera et al. (2008), which was performed both in humans and animals, the human results showed that vitamin C supplementation had no effect on maximal oxygen consumption after 8 weeks of endurance training in sedentary men. However, the most striking results were observed in the animal experiment where vitamin C attenuated training-induced mitochondrial biogenesis and endurance capacity in the rodents. A year later, a study was published where a 6-week aerobic exercise training programme with concomitant antioxidant supplementation (vitamins C and E and lipoic acid) was applied in patients with hypertension (Wray et al., 2009). The results showed enhancement of blood pressure and inhibition of exercise-induced flow-mediated vasodilatation in the supplemented group, indicating detrimental effects of the antioxidant supplements (Wray et al., 2009). In the same year, a human study by Ristow et al. (2009) was published that caused a lot of discussion among the researchers dealing with the same subject. In this study, both sedentary and trained individuals trained for 4 weeks while consuming vitamins C and E. The results showed that the antioxidants inhibited the expected training-induced transcriptional upregulation of genes involved in insulin sensitivity, mitochondrial biogenesis and endogenous antioxidant defence. At the same time that this study was published, one of the current authors and co-workers (Yfanti et al., 2011) were performing an aerobic training study with vitamin C and E supplementation testing some of the same parameters. However, antioxidants during intense cycling exercise had no effect on whole body and skeletal muscle insulin sensitivity or mitochondrial biogenesis in well-trained individuals.

It becomes evident that it is not possible to extract clear conclusions on what is the effect of vitamin C and E supplementation on the adaptive responses to endurance training. The discrepancies among the large number of studies published until now could be attributed to differences in training (i.e. type, duration and intensity), training status of the subjects, supplementation (i.e. type, dosage, duration and timing) as well as the different end points and analytical methods used in each study. Although this particular research area has been extensively studied, additional studies are warranted to obtain more conclusive results on the nutritional antioxidant requirements of professional athletes. Perhaps, more invasive studies should be performed in athletes in order to examine the effect on a molecular level as well as the whole-body level. However, the authors understand that it is difficult to be accepted by professional athletes since such comprehensive investigations interfere with their daily training schedule and recovery.

3.5. IMPLICATIONS FOR ANTIOXIDANT INTAKE IN ATHLETES IN BASIC NUTRITION WITH PARTICULAR FOCUS ON VITAMINS C AND E

On the basis of the data of studies in this area, there is no convincing evidence to recommend antioxidant supplementation during exercise training in addition to the dietary intake of antioxidants. Moreover, on the basis of findings indicating an interference of high doses of supplemental antioxidants with RONS-mediated physiological adaptations to exercise training, caution should be suggested in the use of supplemental antioxidants. Nevertheless, it is very likely that an adequate dietary intake of antioxidants to maintain a physiological antioxidant status is required for athletes undergoing exercise training. In Section 3.5.1, we discuss these antioxidant requirements for

athletes by addressing the question regarding antioxidant amounts. Thereby, particular focus is drawn on vitamins C and E, since most of the research in this field has been investigating the effects of these antioxidants in the context with exercise or, vice versa, the potential effects of exercise on the status of vitamins C and E.

3.5.1. Vitamin C

Vitamin C (ascorbic acid or ascorbate) is an essential micronutrient with numerous biological functions, several of which are particularly important to exercise metabolism and exercise immunology (Peake, 2003; Margaritis and Rousseau, 2008). Beyond its role as a potent hydrophilic antioxidant, vitamin C is a cofactor for various metalloenzymes involved in the biosynthesis of collagen, carnitine, neurotransmitter and peptide hormones (Arrigoni and De Tullio, 2002) as well as a regulation of transcription factors such as AP-1 (Catani et al., 2001), all of which require its properties as a reducing agent (Carr and Frei, 1999; Halliwell and Gutteridge, 2007). Furthermore, ascorbic acid is stored in high concentrations in leukocytes (Levine et al., 1996), and implicated in a number of immune functions such as the (self-) protection of neutrophils from oxidative burst (Gleeson et al., 2004). Considering that these metabolic and immune functions of vitamin C are all related to exercise, it is conceivable that periods of intensified training requiring musculoskeletal growth and repair, as well as an appropriate maintenance of immune function, may increase the requirements of athletes (Peake, 2003; Margaritis and Rousseau, 2008).

Despite some controversies regarding whether changes in the ascorbic acid plasma concentration reflect its actual utilisation by neutralising RONS or other exercise-associated processes, temporary alterations in the ascorbic acid concentration in plasma and leukocytes have been reported following exercise (reviewed by Peake, 2003). Most, but not all (Nieman et al., 2000), of these studies demonstrated an immediate and transient increase of ascorbic acid plasma and/or lymphocyte concentrations after acute bouts of intense endurance (Gleeson et al., 1987; Thompson et al., 2003) and ultra-endurance exercise (Mastaloudis et al., 2004a; Neubauer et al., 2010), perhaps due to a mobilisation of ascorbic acid from the adrenal glands (Gleeson et al., 1987) leukocytes (Viguie et al., 1993) and/or the intake of vitamin C during exercise (Neubauer et al., 2010). Importantly, provided that the investigators monitored time-course dependent recovery responses for a longer period, in several of these studies plasma ascorbic acid concentrations decreased below baseline/pre-exercise values in the days after intense endurance exercise such as a half-marathon (Gleeson et al., 1987) or a marathon (Liu et al., 1999). Hypothetically, the decrease of vitamin C, along with other antioxidants (Neubauer et al., 2010), in the early days of recovery from strenuous, prolonged exercise, in particular if muscle damage and inflammatory responses were induced, may be associated with an increased utilisation of vitamin C due to sustained oxidative stress in the blood (Hessel et al., 2000; Nikolaidis and Jamurtas, 2009) and/or other tissues including skeletal muscle (Peake et al., 2007).

Evidence concerning the chronic effects of exercise training on ascorbic acid concentrations within the plasma or in leukocytes is less conclusive (Peake, 2003). In a recent study (Bergholm et al., 1999), a 3-month training period in marathon runners was accompanied by decreases in all circulating antioxidants measured (including α-tocopherol and β-carotene), except for ascorbic acid, which increased with training. In contrast, in indoor cyclists participating in the Olympic Games (Ferrandez et al., 1996), the ascorbic acid content of lymphocytes and neutrophils decreased immediately prior to the Olympics, concomitantly with increases in serum levels of stress hormones (adrenocorticotropic hormone and β-endorphin), whereas no indications for a suppression of the immune system were found. Importantly, however, antioxidant supplementation at physiological doses (including 120 mg vitamin C) in addition to the dietary antioxidant intake has been shown to preserve the decrease of plasma concentrations of antioxidant vitamins after 4 weeks of overloaded training in well-trained endurance athletes with initially low antioxidant intakes (Palazzetti et al., 2004). The authors of the latter study (Palazzetti et al., 2004) concluded that the amounts of antioxidant vitamins which helped to preserve the status of antioxidant vitamins can easily be provided by a diversified and well-balanced diet. In agreement with these findings, plasma markers of oxidative stress including F2-isoprostanes were significantly lower in response to 40 min of high-intensity exercise when trained athletes maintained their habitual diet, which was rich in antioxidants, compared with a 2-week diet restricted in antioxidants (Watson et al., 2005).

When attempting to define recommendations for vitamin C, it is important to bear in mind its bioavailability and the well-established dose dependency of vitamin C pharmacokinetics (Lykkesfeldt and Poulsen, 2010). As demonstrated in a recent study by Levine et al. (1996) in healthy volunteers, plasma ascorbic acid concentrations reach a plateau at a vitamin C intake of 200 mg per day, whereas the ascorbic acid contents of neutrophils, monocytes and lymphocytes are saturated at a daily intake of 100 mg. Furthermore, this pharmacokinetic study (Levine et al., 1996) indicated that the optimal bioavailability of vitamin C is close to maximum at an intake of 200 mg vitamin C as a single dose, corresponding to the (sigmoid) dose–response curve reaching a plateau steady-state plasma concentration at the same daily intake (i.e. 200 mg). On the basis of the observation that nearly all of the absorbed vitamin C is excreted at a dose of 500 mg, the investigators concluded that there is no evidence for recommending vitamin C doses above 400 mg (Levine et al., 1996). Regarding the safety and toxicity of vitamin C, Levine et al. (1996) considered safe doses of vitamin C to be less than 1000 mg daily, while most health agencies currently agree on a tolerable upper intake level (UL) of 1000–2000 mg daily (Hathcock et al., 2005; Frei et al., 2012), based on reports that adverse health effects tend to occur above 1000 mg of vitamin C per day (Frei et al., 2012).

Current average population recommendations for vitamin C are 75 mg per day for adult women and 90 mg per day for adult men in the United States (Carr and Frei, 1999), and 100 mg/d for both sexes in the German-speaking countries (DACH, 2000). These recommendations are primarily based on biochemical data such as pharmacokinetics, and estimates of stored tissue ascorbic acid supposed to provide adequate antioxidant protection (Carr and Frei, 1999; DACH, 2000; Lykkesfeldt and Poulsen, 2010). In addition, evidence from epidemiological studies, suggesting that a dietary intake of 90–100 mg vitamin C per day is associated with a reduced risk of cardiovascular

disease and cancer, has been taken into account when defining these recommendations (Carr and Frei, 1999; DACH, 2000; Lykkesfeldt and Poulsen, 2010). However, the definition of an optimal vitamin C status remains a matter of debate (Lykkesfeldt and Poulsen, 2010; Frei et al., 2012). Currently, a widely recognised opinion is that the optimum plasma concentration is about the level of saturation, that is, 70 μmol/L (Lykkesfeldt and Poulsen, 2010), which would require a daily intake of about 200 mg vitamin C (Levine et al., 1996). On the basis of the currently available data from human metabolic and pharmacokinetic studies, as well as observational, epidemiologic and randomised placebo-controlled clinical trials, Frei et al. (2012) have proposed 200 mg per day as 'the optimum dietary intake of vitamin C for the majority of the adult population to maximise the vitamin's potential health benefits with the least risk of inadequacy or adverse health effects'.

Concerning the vitamin C status of athletes, a recent cross-sectional study by Rousseau et al. (2004) involving 118 athletes showed that plasma ascorbic acid concentrations were related to energy expenditure, vitamin C intake and gender. These data (Rousseau et al., 2004) indicated that some athletic individuals (e.g. game-sport athletes) did not meet the dietary intake which is proposed to be optimal, mainly due to poor dietary choices (Margaritis and Rousseau, 2008). However, this study also demonstrated that dietary vitamin C intakes of ≥200 mg per day were achieved, particularly by athletes with higher energy expenditure (e.g. endurance athletes) (Rousseau et al., 2004). In support of this study (Rousseau et al., 2004), our data of 42 participants of an Ironman triathlon suggested that requirements of nutritive antioxidants to maintain an adequate physiological antioxidant status (in reference to current recommendations (DACH, 2000)) to a large, if not the full extent, can be achieved by a diversified and well-balanced diet (Neubauer et al., 2010). The study participants were precisely instructed to avoid antioxidant supplementation at larger doses (e.g. not more than 60 mg of vitamin C daily in the form of supplements) throughout the study period in addition to their normal dietary antioxidant intake, which was primarily consumed with foods such as fruits and vegetables. This implicates that the study participants' dietary vitamin C intake was sufficient to maintain a plasma ascorbic acid concentration of 66.6 ± 13.0 μmol/L following a 6-month training period with a weekly net endurance exercise time of 10.7 ± 2.6 h (values are mean ± standard deviation), as assessed in resting conditions 2 days before the Ironman race (Neubauer et al., 2010).

Furthermore, it has been postulated that muscle tissue has a high requirement for, and an increased turnover of, vitamin C (Carr et al., 2013), which is most likely following acute bouts of intense, prolonged exercise and periods of intensified exercise training. Most recently, an investigation of Carr et al. (2013) has provided novel data on the bioavailability of vitamin C in human skeletal muscle. This study (Carr et al., 2013) demonstrated that skeletal muscle is very responsive to vitamin C intake and is strongly related to plasma ascorbic acid concentrations, which indicates that muscle tissue apparently is a relatively labile pool and, perhaps, prone to vitamin C depletion with inadequate intake. Of note, on the basis of an analysis of muscle ascorbic acid status relative to quintiles of plasma ascorbic acid concentrations, the investigators proposed that plasma ascorbic acid concentrations of ≥50 μmol/L should be aimed at to optimise the vitamin C status in the skeletal muscle (Carr et al., 2013), which corresponds to current recommendations for the general population (DACH, 2000).

Taken together, high-dosed supplementation with vitamin C during exercise training cannot be recommended, because there is little evidence of benefits. Moreover, there is growing evidence indicating the potential negative outcomes of antioxidant, and, in particular, vitamin C supplementation on health and performance benefits of exercise training (Khassaf et al., 2003; Gomez-Cabrera et al., 2008). The study of Khassaf et al. indicated that chronic vitamin C supplementation attenuated cellular protective adaptations in response to exercise-induced RONS at a dose of 500 mg per day (Khassaf et al., 2003), although no severe harmful health effects might occur at this dose (Hathcock et al., 2005). However, currently available data suggest that a diet containing antioxidant-rich food is capable of both, maintaining a physiological antioxidant status in competitive athletes during heavy training (Palazzetti et al., 2004; Neubauer et al., 2010), and protecting against exercise-induced oxidative stress (Watson et al., 2005). The question of specific requirements for vitamin C, as for other antioxidants, with exercise training, to date, has not been addressed sufficiently (Margaritis and Rousseau, 2008). However, based on the available data and emerging indications that a plasma concentration of vitamin C of about 70 μmol/L appears to be optimal for health (Lykkesfeldt and Poulsen, 2010), and the vitamin C status of muscle tissue (Carr et al., 2013), a daily intake of about 200 mg of vitamin C to achieve this status (Frei et al., 2012) might serve as an appropriate 'guidance' for athletes. Practical guidelines on how this intake can be achieved are summarised in Table 3.2.

3.5.2. Vitamin E

Vitamin E refers to a group of lipid-soluble compounds including four tocopherols and four tocotrienols (designated as α-, β-, γ- and δ-). Although all of these naturally occurring vitamin E isomers, as well as the synthetic *all rac*-α-tocopherol, have relatively similar antioxidant activities, α-tocopherol (in its natural form also called *RRR*-α-tocopherol) is the most biologically active vitamin E form. The differences in the potency of the different isomeric vitamin E forms *in vivo* mainly result from the preferential recognition of α-tocopherol by the hepatic α-tocopherol transfer protein, upon which α-tocopherol is transferred to lipoproteins and maintained in the plasma and/or delivered to other tissues (Brigelius-Flohe et al., 2002; Traber, 2007; Traber and Atkinson, 2007). Vitamin E was discovered more than 90 years ago as a micronutrient necessary for foetal development in rats (Evans and Bishop, 1922). While its essential functions are still not completely understood, at least one of the major functions of vitamin E is due to its role as a lipid-soluble antioxidant (Halliwell and Gutteridge, 2007). As a potent scavenger of peroxyl radicals, vitamin E is the primary inhibitor of the free radical-mediated chain reaction of lipid peroxidation in mammals including humans (Halliwell and Gutteridge, 2007). The importance of this function is to maintain the integrity of long-chain polyunsaturated fatty acids in the cell membranes throughout the body, and thus maintain their structure and biological function (Brigelius-Flohe et al., 2002; Traber, 2007; Traber and Atkinson, 2007). On the basis of the oxidation theory (Stocker and Keaney, 2004) and the response-to-injury theory (Ross, 1993), which implicate the involvement of oxidative modifications of low-

density lipoproteins and the onset of inflammation in the initiation and progression of atherosclerotic processes, vitamin E is considered to play a key role in the prevention of atherosclerosis and other diseases associated with oxidative stress (Brigelius-Flohe et al., 2002; Roberts et al., 2007). Recently, vitamin E has also been shown to be involved in the regulation of transcription, the release of arachidonic acid (a long-chain polyunsaturated fatty acid and precursor of eicosanoids, which modulates blood vessels and inflammation) and cellular signalling pathways such as protein kinase C signalling (a mechanism regulating cell proliferation and apoptosis) (Brigelius-Flohe et al., 2002; Traber and Atkinson, 2007). However, there is an ongoing debate whether these functions are indeed due to the additional (i.e. non-antioxidant) functioning of vitamin E as a signalling molecule (Brigelius-Flohe et al., 2002) or rather related to its antioxidant and membrane-protecting capabilities (Traber and Atkinson, 2007).

Given the antioxidant and protective functions of vitamin E, it is not surprising that many investigators in the field have focused on the potential of vitamin E supplementation to counteract exercise-induced oxidative stress and to protect against exercise-induced muscle damage (Jackson et al., 2004; Peternelj and Coombes, 2011). Although there is no consistent evidence for beneficial effects of supplemented vitamin E in the context with exercise, as outlined in our literature overview above, it is well known that the integrity of muscle cells requires an adequate α-tocopherol status (Coombes et al., 2002; Jackson et al., 2004; Margaritis and Rousseau, 2008). When addressing the question regarding requirements for vitamin E during exercise training, however, it is important to note that the assessment of tissue levels of antioxidants, in particular vitamin E, is associated with limitations (Margaritis and Rousseau, 2008; Powers and Jackson, 2008). Exercise training (especially endurance training) is associated with an increase in high-density lipoproteins (Durstine et al., 2001) as main carriers of plasma α-tocopherol, and the cellular vitamin E uptake is related to lipoprotein metabolism (Mardones and Rigotti, 2004). Therefore, it has been hypothesised that certain mechanisms responsible for the incorporation of α-tocopherol into muscle cells could be enhanced due to training (Margaritis and Rousseau, 2008).

In response to acute bouts of endurance (Aguilo et al., 2005) and ultra-endurance exercise (Mastaloudis et al., 2001; Neubauer et al., 2010), increased plasma concentrations of α-tocopherol were observed. This mobilisation of α-tocopherol might be associated with exercise-induced changes in the lipoprotein metabolism, perhaps rather reflecting a shift from tissue stores to plasma circulation rather than a response to the intake of vitamin E during prolonged exercise (Mastaloudis et al., 2001, 2004a). Moreover, similar to plasma concentrations of vitamin C and other nutritive antioxidants, γ-tocopherol decreased temporarily 1 day after an Ironman triathlon, while the decrease in α-tocopherol was not significant (Neubauer et al., 2010). In contrast, Mastaloudis et al. (2004a) reported a prolonged decrease of α-tocopherol (corrected for plasma lipids) from 3 days after a 50-km ultra-marathon run on until 6 days thereafter, regardless of whether the study participants were supplemented with vitamin C and *RRR*-α-tocopheryl acetate or not. In a previous study (Mastaloudis et al., 2001), Mastaloudis and co-workers observed an increased rate of vitamin E turnover (assessed by deuterium-labelled vitamin E) in response to the same ultra-marathon race compared with resting conditions, which the authors attributed not only to an increased lipoprotein turnover, but also to increased oxidative stress. In an attempt to assess the functional status of vitamin E in trained runners, Cases et al. (2006) showed that plasma α-tocopherol concentrations neither increased after a half-marathon run nor after supplementation with an almond-based beverage moderately enriched with vitamins E and C. However, this study indicated that α-tocopherol concentrations in circulating lymphocytes increased in response to the half-marathon in the supplemented and the non-supplemented group, whereas the post-exercise α-tocopherol content in the neutrophils increased in the supplemented group only (Cases et al., 2006). This supports the idea that vitamin E is re-distributed during acute strenuous exercise. Finally, whereas α-tocopherol plasma concentrations decreased in response to a 3-month marathon training period (Bergholm et al., 1999), available data on vitamin E levels in human skeletal muscle suggest that chronic exercise does not alter vitamin E concentrations in the muscle (Tiidus et al., 1996).

As discussed above, potential limitations have to be considered when interpreting the vitamin E status of athletes based on plasma concentrations (Margaritis and Rousseau, 2008). However, it is notable that the (resting) plasma α-tocopherol concentrations in 42 Ironman triathletes following a 6-month training period and prior to the Ironman race were 22.66 ± 13.0 μmol/L (Neubauer et al., 2010), that is, in a normal physiological range (Traber, 2007), but moderate in reference to the current recommended values for the general population (i.e. 30 μmol/L) (DACH, 2000). Furthermore, in agreement with a recent cross-sectional study in well-trained athletes (Rousseau et al., 2004), high inter-individual variations among the Ironman triathletes were observed (Neubauer et al., 2010). These data, in addition to observations that the intake of vitamin E among well-trained athletes is often below the recommendations for the general population (Rousseau et al., 2004; Margaritis and Rousseau, 2008), suggest that the vitamin E intake of athletes requires specific attention.

The current dietary reference intake (DRI) for vitamin E (or α-tocopherol-equivalents) is 15 mg per day for both sexes in the United States (Food and Nutrition Board, 2000), and 14–15 mg per day for adult men and 12 mg per day for adult women in the German-speaking countries (DACH, 2000). Owing to insufficient information on more specific functions of vitamin E, these (estimated) guidelines are largely based on the antioxidant activity of vitamin E and its role to protect mono- and polyunsaturated fatty acids from lipid peroxidation (DACH, 2000; Traber, 2001; Brigelius-Flohe et al., 2002). Recent data from prospective, randomised, placebo-controlled clinical trials focused on the potential of vitamin E supplementation in the prevention or modulation of diseases supposedly associated with oxidative stress are inconsistent (reviewed by Brigelius-Flohé et al., 2002). These data convinced neither the Panel of Dietary Antioxidants of the US Food and Nutrition Board nor the German-speaking authorities to recommend an increase of more than 3 mg (Food and Nutrition Board, 2000), or more than 5 mg of vitamin E (or α-tocopherol-equivalents) per day (DACH, 2000) compared with previous recommendations. Furthermore, some of these studies raised health concerns about the long-term safety of high-dosed vitamin E supplementation, and there is an ongoing debate about the toxicity of vitamin E. The US authorities have set the UL at 1000 mg of vitamin E (or α-tocopherol-equivalents) per day (Hathcock et al., 2005). In contrast, authorities in the German-speaking countries have considered potential adverse

effects (an increased incidence of bleeding in combination with medication for antiplatelet activity) at doses between 200 and 800 mg of vitamin E (or α-tocopherol-equivalents) for their safety assessment (DACH, 2000). Crucially, in the context with exercise training, detrimental effects have been reported at daily doses of 180 mg of α-tocopherol-equivalents (400 IU vitamin E) in combination with 500 mg vitamin C (Ristow et al., 2009).

Until more specific evidence is available on the vitamin E requirements of exercising individuals and athletes, they should adhere to both the DRIs for the general population and a plasma α-tocopherol concentration of ≥30 μmol/L, which is considered as beneficial in preventing cancer and cardiovascular disease (DACH, 2000). Importantly and largely in agreement with the DRI (DACH, 2000), the vitamin E intake required during training periods of increased intensity and/or volume might be somewhat above 15 mg per day. As discussed above, the current DRI for vitamin E is based on its potential to protect unsaturated fatty acids, requiring 0.06, 0.04, 0.6, 0.8, 1.0, 1.2 mg of α-tocopherol-equivalents per gram mono-, double-, triple-unsaturated fatty acids, and so on in addition to a basic requirement of 4 mg α-tocopherol-equivalents (DACH, 2000). Considering that typical endurance training requires 500–900 kcal per hour (Jeukendrup, 2008) and that the total energy expenditure (TEE) of endurance athletes can easily increase to ≥4.000 kcal per day, this also increases the DRI for both unsaturated fatty acids and vitamin E. For example, for an athlete with a daily TEE of 4000 kcal, the DRI for monounsaturated fatty acids (i.e. 13% of the TEE) increases to ca. 57.8 g of ω-9-fatty acids, whereas the DRI for the essential polyunsaturated fatty acids (i.e. 2.5% and 0.5% of the TEE for ω-6- and ω-3-fatty acids, respectively) increases to ca. 25.8 g of ω-6- and 5.2 g of ω-3-fatty acids. Provided that athletes achieve these DRIs for unsaturated fatty acids, the DRI for vitamin E concomitantly increases to 24 mg α-tocopherol-equivalents per day. On the basis of these considerations, it is reasonable to suggest a range between 12 and 24 mg of vitamin E (or α-tocopherol-equivalents) per day for female athletes and between 14 and 30 mg for male athletes as proxy ‘guidance’.

In view of the discussed detrimental effects of high-dosed vitamin E supplementation, athletes should be encouraged to abstain from supra-physiological doses of vitamin E, but be encouraged to increase their dietary vitamin E intake. The latter requires a substantial increase in the consumption of foods that are rich in fats, such as nuts, margarine and certain oils. This is also supported by the food frequency questionnaire data gained from the study in the Ironman participants, indicating that the plasma α-tocopherol concentration was highest (i.e. 29.6 ± 6.6 μmol/L) in the subject group that reported a daily intake of nuts (Neubauer et al., 2010). Practical guidelines for the vitamin E intake in the athlete’s basic nutrition are summarised in Table 3.2.

3.6. GENERAL CONCLUSIONS ON THE INTAKE OF ANTIOXIDANTS IN THE ATHLETE’S BASIC NUTRITION

The general picture that emerges from the available data on antioxidant requirements of athletes is that the antioxidant intake during exercise training to maintain an appropriate physiological antioxidant status in reference to current recommendations can be achieved by consumption of a balanced and well-diversified diet. The potential and importance of dietary sources of antioxidants to achieve these goals has been demonstrated even during very committed endurance training programmes (e.g. training for long-distance triathlon races) (Neubauer et al., 2010). Moderate and timely limited antioxidant supplementation may be warranted in specific situations, for example, during periods of intensified training, during acute bouts of intense endurance exercise lasting several hours and in the early recovery period thereafter or during energy restriction/weight loss programmes. Nevertheless, the ultimate goal in the athlete’s basic nutrition is certainly to optimise the nutrition. Crucially, the optimal bioavailability and combined action of multiple phytochemical and antioxidant compounds derived from fruits, vegetables, whole grains and nuts cannot be replaced by supplementation (DACH, 2000). Furthermore, while phytochemicals such as polyphenols are well recognised for their antioxidant properties, their beneficial physiological effects may be promoted by a multitude of mechanisms (Halliwell, 2009; Hawley et al., 2011).

The current literature is not sufficient to determine definitive recommendations concerning antioxidant requirements for athletes and exercising individuals. However, based on available data, it is feasible to suggest that these requirements, particularly for vitamins C and E, might be in a range of ≥100–200% of the current recommendations for the general population. Whereas an intake of ca. 12–30 mg of vitamin E requires specific attention (see Table 3.2), it is likely that by meeting the ‘guidance’ of 200 mg vitamin C per day, athletes may also achieve an appropriate intake of other antioxidative nutrients and phytochemicals, since the vitamin C plasma status serves as a proxy or surrogate marker for vegetable and fruit intake (Lykkesfeldt and Poulsen, 2010). Additional research is warranted to define antioxidant requirements during exercise training, which should also take into account nutrigenomic issues (Peternelj and Coombes, 2011). Finally, it is important to note that nutritional guidelines, in particular, for athletes need to be fine-tuned on an individual basis.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

ACKNOWLEDGEMENTS

The authors acknowledge Prof. Bente Klarlund Pedersen, Centre of Inflammation and Metabolism, Denmark, for a critical review of the chapter, and Assistant Professor Petra Rust, Department of Nutritional Sciences, University of Vienna, Austria, for support with the calculations for the representative daily intakes of vitamins C and E.

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Tables

TABLE 3.1

Overview on Studies on Antioxidant Supplementation in Exercise Training

Reference	Subjects (Training Status, N, Sex)	Type of Training	Duration of Training (Weeks)	Acute Exercise	Supplementation (Type, Dosage)/Daily	Duration of Supplementation (Weeks)	Parameters Tested	Results of Supplementation
Gey et al. (1970)	Well-trained, N = 286	Unspecified	12		1000 mg vitamin C	12	Endurance (12 min field test)	No effect
Lawrence et al. (1975)	Trained (swimmers), N = 48	Unspecified	24		900 IU vitamin E	24	Endurance	No effect
Sharman et al. (1976)	Moderately trained (swimmers), N = 27, M/F	Endurance and interval	6		270 IU vitamin E	6	Cardiorespiratory efficiency, motor fitness	No effect
Rokitzki et al. (1994)	Athletes (runners), N = 24	Endurance		Marathon race	400 IU vitamin E, 200 mg vitamin C	4.5	Muscle damage	Beneficial effect
							Lipid peroxidation	No effect
							Antioxidant enzymes	No effect
Zoppi et al. (2006)	Athletes (soccer), N = 10, M	Endurance, strength, anaerobic	12		1000 mg vitamin C, 530 IU vitamin E	12	Antioxidant enzymes	No effect
							Protein oxidation	No effect
							Lipid peroxidation	Beneficial effect
							Muscle damage	Beneficial effect
Mastaloudis et al. (2004a)	Trained (runners), N = 22, M/F	Unspecified	–	50 km ultramarathon	1000 mg vitamin C, 200 IU vitamin E	6	Lipid peroxidation	Beneficial effect
							Inflammation	No effect
Yfanti et al. (2010)	Trained (cycling), N = 21, M	Endurance (cycling)	12		500 mg vitamin C, 400 IU vitamin E	16	VO_{2max}	No effect
							Lactate	No effect
							Glycogen	No effect
							Metabolic enzymes	No effect
							Antioxidant enzymes	No effect
Yfanti et al. (2012)	Trained (cycling), N = 21, M	Endurance (cycling)	12		500 mg vitamin C, 400 IU vitamin E	16	Lipid peroxidation	Detrimental effect
							Protein oxidation	Detrimental effect
Nieman et al. (2004)	Athletes (triathlon), N	Endurance	8	Ironman triathlon race	800 IU vitamin E	8	Lipid peroxidation	Detrimental effect

	= 38, M/F							
							Inflammation	Detrimental effect
Knez et al. (2007)	Athletes (half and full Ironman triathletes), N = 29, M/F	Endurance	~312	Half-distance and full Ironman triathlon race	560 mg vitamin C, 470 IU vitamin E	~208	Lipid peroxidation	Detrimental effect
							Antioxidant enzymes	No significant effect
Lamprecht et al. (2009)	Athletes (cyclists), N = 8, M	Endurance		30 and 60 min cycling test	107 IU vitamin E, 450 mg vitamin C, 36 mg β-carotene, 100 μg selenium	2	Lipid peroxidation	Detrimental effect
Mastaloudis et al. (2004b)	Trained (runners), N = 21, M/F	Unspecified		50 Km ultramarathon	1000 mg vitamin C, 270 IU vitamin E	6	DNA damage	No significant to detrimantal effect
Khassaf et al. (2003)	Untrained, N = 16, M			45 min cycling	500 mg vitamin C	8	Antioxidant enzymes	No significant effect
							HSPs	Detrimental effect
Fischer et al. (2006)	Moderately trained, N=21, M			3 h knee-extensor exercise	500 mg vitamin C, 400 IU vitamin E (α-tocopherol), or 500 mg vitamin C, 292 IU vitamin E (α-tocopherol), 130 IU vitamin E γ-tocopherol	4	HSP72	Detrimental effect
Palazzetti et al. (2004)	Athletes (triathlon), N = 17, M	Endurance	8	Duathlon test	150 mg selenium, 120 mg vitamin C, 2000 IU vitamin A, 30 IU vitamin E	8	Antioxidant enzymes	Beneficial effect
Gomez-Cabrera et al. (2008)	Human study: Sedentary, N = 14, M	Endurance	8		1000 mg vitamin C	8	VO_{2max}	No effect
	Animal study: N = 18	Endurance	3–6		500 mg/kg body weight vitamin C	3–6	Endurance	Detrimental effect
							VO_{2max}	No effect
Wray et al. (2009)	Sedentary hypertensive, N = 6, M	Endurance	6		600 mg lipoic acid, 1000 mg vitamin C, 600 IU vitamin E	6	Blood pressure	Detrimental effect
Ristow et al. (2009)	Trained, N = 20, M and Untrained, N = 19, M	Endurance and strength	4		1000 mg vitamin C, 400 IU vitamin E	4	Insulin sensitivity	Detrimental effect
							Mitochondrial biogenesis	Detrimental effect

							Antioxidant enzymes	Detrimental effect
Yfanti et al. (2011)	Trained (cycling), N = 21, M	Endurance (cycling)	12		500 mg vitamin C, 400 IU vitamin E	16	Insulin sensitivity	No effect
							Mitochondrial biogenesis	No effect

Note: 1 IU vitamin E = 0.67 mg *RRR*-α-tocopherol = 1 mg *all rac*-α-tocopheryl acetate.

Abbreviations: M = male; F = female; mg = milligram, IU = international units.

TABLE 3.2

Practical Guidelines for the Intake of Antioxidants in the Athlete's Basic Nutrition

General Guidelines
• The requirements for nutritive antioxidants, in particular vitamins C and E, during exercise training are supposed to be in a range of ca. ≥100–200% of the current recommendations for the general population, dependent on training loads (e.g. intensity, volumes and frequency of the training). The general picture that emerges from the available data is that the antioxidant intake during exercise training to maintain an appropriate physiological antioxidant status in reference to current recommendations can be achieved by consumption of a balanced and well-diversified diet.
• There is no convincing evidence to recommend antioxidant supplementation during exercise training. High dosed antioxidant supplementation can interfere with physiological training adaptations mediated by reactive oxygen/nitrogen species. Therefore, optimizing the nutrition appears to be the wisest option.
• Athletes should be encouraged to consume a diet rich in antioxidants containing a broad variety of fresh fruits, raw and/or steam-cooked vegetables, fruit and vegetable juices, whole grains and nuts. To meet the suggested intake of vitamin E, an increased intake of nuts, margarinecertain oils including wheat germ oil, sunflower oil corn oil and rapeseed oil is required.
• During periods with a higher training volume and/or a higher training intensity, there might be an increased requirement for antioxidants, which can be achieved through the increased daily energy expenditure and an increased food intake, provided that the nutrient density is appropriate. In particular, an increased consumption of fruit- and vegetable juices can help in such training situations to match increased requirements for energy, carbohydrates and antioxidants.
• Moderately dosed and timely limited antioxidant supplementation and/or the use specialized sports products (e.g. beverages, carbohydrate-rich bars, gels, etc.) fortified with antioxidants may be warranted in specific situations such as during acute bouts of intense endurance exercise lasting several hours and in the early recovery period (within ca. 24 hours) thereafter, or during energy restriction/weight loss programs. However, high dosed antioxidant supplementation, i.e. >>100% of the recommended dietary allowance (RDA)/dietary reference intake (DRI), in addition to the dietary intake of antioxidants, should be avoided.
• Nutritional guidelines for athletic populations need to be fine-tuned through individualized nutritional advice from appropriate professionals, which includes a comprehensive nutritional assessment and blood analysis.
Example How to Achieve an Appropriate Intake of Vitamin C
A daily intake of about 200 mg of vitamin C to is suggested as an appropriate 'guidance' for athletes.
Exemplarily, 228 mg of vitamin C can be provided by a diet including 200 g of an apple (≈24 mg vitamin C) 45 g of a kiwi-fruit (≈20 mg vitamin C), 50 g of a green capsicum (≈39 mg vitamin C), 100 g of a mixture of steam-cooked vegetables (≈45 mg vitamin C) and 200 mL of fresh orange juice (≈100 mg vitamin C).
Example How to Achieve an Appropriate Intake of Vitamin E
A daily intake of about 12–24 mg of vitamin E (or α-tocopherol-equivalents) for female athletes14–30 mg for male athletes is proposed as proxy 'guidance', dependent on the daily energy expenditure and the intake of polyunsaturated fatty acids, both of which are commonly increased in the athletic population compared with the general population.
Exemplarily, 25 mg of vitamin E (or α-tocopherol-equivalents) could be provided by a diet including 200 g of rye bread with oil seed ingredients (≈7 mg α-tocopherol-equivalents), 200 g of muesli (≈6 mg α-tocopherol-equivalents), 25 g of a nut mixture of walnuts, hazelnuts and almonds (≈4 mg α-tocopherol-equivalents), 10 g of rapeseed oil (≈2 mg α-tocopherol-equivalents) and 10 g of sunflower oil (≈6 mg α-tocopherol-equivalents).
Nutritional analyses were performed using Nut.s nutritional software v1.31.33, based on the German/Austrian Food database BLS-Version 3.01.

Bookshelf ID: NBK299049 PMID: 26065088