运动训练中补充抗氧化剂:有益还是有害?

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摘　要: 运动过程中骨骼肌产生的高水平反应物会导致肌肉损伤和肌肉功能受损,一般认为补充抗氧化剂可以保护肌肉不受损伤。无论对于运动爱好者还是专业运动员,抗氧化剂都是最常用的运动补剂之一。目前备受关注的是用额外口服抗氧化剂的方法来支持内源性防御系统,从而实现预防或减轻氧化应激、减少肌肉损伤并改善运动表现。目前有大量已发表的研究对该主题进行了讨论, 大多数研究表明,抗氧化剂可以减轻运动引起的氧化应激,但大多数研究都未发现其对肌肉损伤和肌肉功能有任何影响。此外,越来越多的证据表明,抗氧化剂对健康和训练适应有消极作用。本文深入分析总结了关于活性物质(Reactive Species)在体内的作用以及服用抗氧化剂对维持健康和提高身体性能的功效的文献。

关键词: 活性物质;抗氧化剂;运动补剂;运动表现;线粒体
中图分类号:G804.5　　文献标志码: A　文章编号:1006-1207(2019)01-0001-21
DOI:10.12064/ssr.20190101

Antioxidant Supplementation during Exercise Training: Beneficial or Detrimental?

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Abstract: High levels of reactive species produced in skeletal muscle during exercise have been associated with muscle damage and impaired muscle function, whereas antioxidants are seen as the defense against these threats. Antioxidants are among the most common sports supplements used by amateur and professional athletes. Supporting endogenous defense systems with additional oral doses of antioxidants has received much attention as a strategy to prevent or reduce oxidative stress, decrease muscle damage, and improve exercise performance. There have been numerous studies published on this topic. A majority of the studies demonstrated that antioxidant supplementation would attenuate exercise-induced oxidative stress, yet most of them reported no effects on muscle damage and performance. Moreover, a growing body of evidence indicates detrimental effects of antioxidant supplementation on health and training adaptations. This review provides an in-depth review of literature concerning the role reactive species play in the body and the efficacy of taking antioxidant supplementation for maintaining health and enhancing performance.

Key Words: reactive species; antioxidants; sports supplements; sports performance; mitochondria

0　前言

在运动过程中,由于新陈代谢增加,氧利用率升高,从而导致高活性氧从线粒体渗漏[1]。除此之外,肌肉收缩本身也会激活磷脂酶 A2, 启动一系列酶,从而引起活性物质的增加[2]。活性氧会改变细胞结构和功能,并导致肌肉损伤、免疫功能障碍和身体疲劳[3]。在过去的 40 年中,我们对运动所引起的氧化应激生物学意义的讨论迅速增加。现在我们认识到,

0　Introduction

During exercise, metabolism increases and oxygen utilization is elevated, leading to leakage of highly reactive oxygen species from mitochondria[1]. Aside from mitochondrial leakage, contraction itself activates phospholipase A2, initiating a cascade of enzymes and thereby increasing reactive species[2]. Reactive oxygen species alter cell structure and function, and contribute

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收稿日期: 2018-12-09

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虽然高水平的自由基会损伤细胞成分，但中低水平的氧化剂在细胞中发挥多种调节作用，如控制基因表达、调节细胞信号通路和调节骨骼肌力量输出[4]，同时也可以刺激糖原再合成[5]、降低感染的风险[6]，甚至可以通过启动和促进对训练的适应性反应来提高运动成绩[7-10]。活性物质有害还是有益，取决于个体的运动持续时间、运动强度、身体属性和营养状况[11]。

无论是专业运动员还是运动爱好者，摄入抗氧化剂都是常见的做法。尽管并没有证据证明其益处，但各种营养补充剂的市场依旧十分巨大[12]。事实上，抗氧化剂是专业运动员和运动爱好者最常使用的运动补充剂之一[13-14]。虽然这些产品已被吹捧为预防运动引起的氧化损伤和提高运动表现的手段，但对于其功效依旧缺乏证据。此外，一些研究表明抗氧化剂对受过训练者的健康和运动表现有不良影响[15-16]。越来越多的证据表明，自由基在细胞中扮演重要的生理功能，并且抗氧化剂和自由基之间的平衡是获得生理适应性的必要前提[17-20]。因此，我们有必要评估如何谨慎使用抗氧化剂，特别是在专业运动员中。

本综述旨在提供研究证据，证明抗氧化剂在改善健康和运动表现方面的功效。文章开篇是有关活性物质、抗氧化防御系统和运动诱导的氧化应激的概述。接下来是关于活性物质在调节训练导致的适应性中的作用以及抗氧化剂对运动表现影响的文献综述。文章最后还提供了有实际证据支撑的建议，从而帮助专业运动员或运动爱好者在补充抗氧化剂上作出明智的决定。

1　细胞内主要活性物质的产生

自由基一词是指活性氧和氮类物质，由于携带未配对的价电子而具有高活性。在动物肌肉纤维中，5种主要自由基具有生物学影响。第一种是过氧化物（O_2^-），在线粒体和细胞质中形成，通过线粒体中电子传递链的少量氧分子提前释放为O_2^-[21]。在黄嘌呤转化为尿酸过程中，还原型辅酶Ⅰ，或黄嘌呤氧化酶（XO）也可在细胞外间隙形成O_2^-。XO主要存在于微血管内皮细胞中，但也存在于白细胞中，剧烈运动后可能渗入肌纤维[22]。第二种是过氧化氢（H_2O_2），可以在XO转化次黄嘌呤–黄嘌呤尿酸过程中释放，也可以通过线粒体、胞质溶胶和细胞外间隙中的过氧化物歧化酶（SOD）亚型由O_2^-形成[23-24]。第三种是羟基自由基（OH），通过O_2^-或H_2O_2与金属离子如铁或铜反应形成[24]。第四种是一氧化氮（NO），由L-精氨酸通过一氧化氮合酶（NOS）形成，主要是骨骼肌中的神经元亚型（nNOS）与内皮型NOS（eNOS）[25-26]。最

to muscle damage, immune dysfunction, and fatigue[3]. During the past four decades, our knowledge about the biological implications of exercise-induced oxidative stress has expanded rapidly. It is now appreciated that while high levels of free radicals can damage cellular components, low-to-moderate levels of oxidants play multiple regulatory roles in cells such as the control of gene expression, regulation of cell signaling pathways, and modulation of skeletal muscle force production[4]. They can also be involved in stimulating glycogen re-synthesis[5], reducing susceptibility to the risk of infection[6], and they may even enhance athletic performance by initiating and promoting adaptive responses to training[7-10]. The extent to which reactive species are damaging or helpful depends on the exercise duration, intensity, fitness attributes and nutritional status of the individual[11].

Antioxidant supplementation is a common practice amongst both professional athletes and physically active individuals, and the market offering various nutrient supplements is immense despite the unclear evidence of their benefits[12]. Indeed, antioxidants are among the most common sports supplements used by amateur and professional athletes[13-14]. Although these products have been touted as a means of preventing exercise-induced oxidative damage and enhancing performance, consistent evidence of their efficacy is lacking. Moreover, some studies suggest adverse effects of antioxidant supplementation on the health and performance of trained individuals[15-16]. There is a growing body of evidence that the appearance of free radicals fulfils important physiological functions in cells, and that a balance between antioxidants and free radicals is necessary for desired physiological adaptations[17-20]. Thus, it becomes necessary to evaluate the prudence of antioxidant supplementation, particularly among athletes.

This review is to provide research evidence with regard to the efficacy of using antioxidant supplementation in improving health and sports performance. The article begins with an overview of reactive species, antioxidant defense systems, and the exercise-induced oxidative stress. This is then followed by a review of literature concerning the role reactive species play in mediating training-induced adaptations and the effect of antioxidant supplementation on exercise performance.

后一种是过氧自由基过氧亚硝酸盐（$ONOO^-$），当 O_2^- 与 NO 反应时在胞质溶胶中形成[27]。因为它们的起源是紧密相连的，运动时电子传递链和 NOS 的活化导致这 5 种自由基各自的数量增加。

底物消耗会导致谷胱甘肽还原酶活性下降，高温会加速线粒体解偶联。这两者也可能促进运动过程中自由基的产生。此外，会导致酸中毒的无氧运动带来的短暂缺氧，可能增加氧化应激反应[28]。最后，运动的机械应力本身，如外部冲击，肌肉对骨骼的牵拉，肌肉的离心收缩和肌肉之间的摩擦等，也可以促进自由基的形成[29]。

2 活性物质的利弊

细胞和细胞外空间暴露在来自外源和内源的大量活性物质中。外源性活性物质来源包括氧气、辐射、空气污染物、异生素、药物、酒精、重金属、细菌、病毒、日光、食物和运动等。尽管如此，内源性活性物质来源更重要也更广泛，因为在整段生命过程中它会持续产生。

作为正常代谢的一部分，所有需氧细胞都会产生活性物质。活性物质在疾病的发生、发展中发挥着重要作用[30]。活性氧和活性氮由于具有高活性，能够使其他生物学层面上重要的分子发生变形，从而损伤细胞结构，阻碍细胞功能的实现。O_2^-、H_2O_2 和 OH 能够获得不饱和脂肪酸中与双键相邻的质子，如细胞膜中的质子。于是这些脂肪酸形变的连锁反应开始，形成脂质过氧化物。这个过程称为“脂质过氧化”，会导致细胞膜功能不良[24]。脂质双分子层的破坏改变了细胞膜的流动性和通透性，并可能导致膜结合蛋白活性降低[31]。NO 可以氧化蛋白质并改变其结构，从而损害其功能并影响基因转录[25,32-35]。同样，OH、NO 和 $ONOO^-$ 可以氧化核苷酸，损伤 DNA，从而导致肿瘤的出现[36]。NO 也被认为对肌纤维的收缩性有直接的抑制作用[37]。最后，氧化损伤也导致炎症[38]和细胞凋亡[39]，并可能最终导致细胞功能下降。

虽然自由基一般只被看作是对细胞的威胁，但这种片面的想法也开始受到挑战。越来越多的证据表明，自由基在调节肌肉适应过程中对氧化还原敏感的信号通路发挥重要作用[40]。最近几项动物研究以及一些涉及运动员的研究提出了相关框架，涉及包括 O_2^-、H_2O_2 和 NO 在内的活性物质作为重要细胞信号的功能作用。有氧耐力训练后，丝裂原活化蛋白激酶信号通路的活化可增强线粒体生物合成和毛细血管化（血管生成）、肌肉增殖和葡萄糖转运能力[19,41]。人们已经发现，这些对训练的适应可能依赖于自由

The article also offers evidence-based recommendations that help athletes or those who are physically active in making a wise decision on antioxidant supplementation.

1 Production of Major Reactive Species in Cells

The term free radical refers to reactive oxygen and nitrogen species, which are highly reactive because of an unpaired valence electron. In animal muscle fibers, five main radicals have a biological impact. The first, superoxide (O_2^-), is formed in mitochondria and in the cytosol. A small amount of molecular oxygen passing through the electron transport chain in mitochondria is prematurely released as O_2^-[21] Superoxide can also be formed in the extracellular space by nicotinamide adenine dinucleotide phosphate hydrogen oxidase or by the enzyme xanthine oxidase (XO) during the conversion of xanthine to uric acid. XO is found mostly in microvascular endothelial cells, but is also present in leucocytes, which may infiltrate muscle fibers following strenuous exercise[22]. The second, hydrogen peroxide (H_2O_2), can be released during the hypoxanthine → xanthine → uric acid conversion by XO, or it can be formed from O_2^- by superoxide dismutase (SOD) isoforms in mitochondria, cytosol, and the extracellular space [23-24]. Third, the hydroxyl radical (·OH) is formed when O_2^- or H_2O_2 reacts with metal ions such as iron or copper[24]. The fourth radical, nitric oxide (NO·), is formed from L-arginine by nitric oxide synthase (NOS), mainly the neuronal isoform (nNOS) in skeletal muscle, but also endothelial NOS (eNOS)[25-26]. Lastly, the peroxyl radical, peroxynitrite ($ONOO^-$), is formed in the cytosol when O_2^- reacts with NO·[27]. Because their origins are closely linked, increased activation of the electron transport chain and NOS during exercise leads to elevated production of each of these five radicals.

Substrate depletion, leading to a fall in glutathione reductase activity, and hyperthermia, which promotes mitochondrial uncoupling, may also contribute to free radical production during exercise. Furthermore, transient hypoxia during anaerobic exercise leading to acidosis may increase oxidative stress[28]. Finally, mechanical stress of exercise, such as grinding, shearing, bending, and cutting, can itself increase free radical formation[29].

基引起的细胞氧化还原电位的改变[40]或 O_2^- 的短暂出现[17-18]，因为这些似乎刺激了该通路内某些重要转录因子的上调。

另外，胞外间隙中由 O_2^- 形成的 H_2O_2 起到血管扩张剂的作用，可以优化血流速度。一氧化氮合成酶在内皮细胞中产生的 NO 也会带来支持收缩肌的动脉血管舒张[42]，从而导致血流速度增加[43]。由此而引起的肌纤维微血管剪切应力的增加可刺激肌肉血管生成[44]。内源性氧化剂防御，特别是 O_2^-，也因活性氧的负反馈而上调[19,45]。

自由基也可能有急性积极作用。低浓度时，它们有助于维持肌肉力量输出[40]。此外，在吞噬作用的氧爆过程中，巨噬细胞释放 O_2^-、H_2O_2 和 NO，作为清除受损或死亡细胞物质的一部分，这有助于加快修复过程[46]。

3 抗氧化防御系统

为了对抗活性物质，生命机体配备了高效的抗氧化防御系统。这些包括非酶、酶和膳食抗氧化剂。谷胱甘肽、尿酸、硫辛酸、胆红素和辅酶 Q10 等都是非酶类抗氧化剂，这些抗氧化剂是内源性的，通常是细胞代谢的副产物。主要的酶抗氧化剂是 SOD，过氧化氢酶，谷胱甘肽过氧化物酶（GPX）和谷胱甘肽还原酶，而大多数已知的膳食抗氧化剂是生育酚（维生素 E）、抗坏血酸（维生素 C）和类胡萝卜素（β- 胡萝卜素）。此外，各种多酚化合物近年来已被推广为营养抗氧化剂。在涉及抗氧化剂的研究中，α- 硫辛酸和药物如 N- 乙酰半胱氨酸和别嘌呤醇也受到了评估。

在人体骨骼肌纤维中，几种内源性酶和底物共同作用从而清除自由基。SOD 将 O_2^- 还原成 H_2O_2。在细胞溶质中，H_2O_2 随后可以通过 GPX 转化为水，或通过硫氧还蛋白而形成过氧化物氧还酶。H_2O_2 也可能通过过氧化氢酶转化为水和分子氧[26]。二肽肌肽和丝氨酸也通过清除 O_2^- 和 OH[47]起到抗氧化剂的作用。

不在人体内合成的非酶促抗氧化剂，必须从外源获得，包括维生素 A（β- 胡萝卜素）、维生素 C（抗坏血酸）和维生素 E（α- 生育酚），这些维生素也被称为膳食抗氧化剂。这些物质能够通过质子捐赠清除各种自由基。维生素 A 属于一组称为类胡萝卜素的红色、橙色和黄色色素[48]。其他包括 α- 胡萝卜素、β- 隐黄质、番茄红素、叶黄素和玉米黄质。β- 胡萝卜素是活性最强、最活跃的类胡萝卜素，被食用后，它转化为视黄醇，这是一种易于使用的维生素 A。除了

2 Negative and Beneficial Roles of Reactive Species

Cells and extracellular spaces are exposed to a large variety of reactive species from both exogenous and endogenous sources. The exogenous sources include exposure to oxygen, radiation, air pollutants, xenobiotics, drugs, alcohol, heavy metals, bacteria, viruses, sunlight, food, and exercise. Nonetheless, exposure to endogenous sources is much more important and extensive because it is a continuous process during the life span.

Reactive species are generated by all aerobic cells as part of normal metabolism. The effect of reactive species plays an important role in the development of diseases[30]. Because of their high reactivity, reactive oxygen species and reactive nitrogen species are able to deform other biologically important molecules, thus causing damage to cell structure and obstructing cell function. Superoxide, H_2O_2, and ·OH are able to acquire the protons adjacent to double bonds in unsaturated fatty acids, such as those in cell membranes. This begins a chain reaction of deformation to these fatty acids forming lipid peroxides. This process, called "lipid peroxidation", results in poorly functioning cell membranes[24]. The disruption of the lipid bilayer changes fluidity and permeability of the cell membrane and may lead to inactivity of membrane bound proteins[31]. NO· can oxidize proteins and alter their structure, thereby impairing their function and affecting genetic transcription[25,32-35]. Similarly, ·OH, NO·, and $ONOO^-$ can oxidize nucleotides causing damage to DNA, which can lead to tumors[36]. NO· has also been suggested to have a direct inhibitory effect on contractility in muscle fibers[37]. Finally, oxidative damage also promotes inflammation[38] and apoptosis[39] and may eventually lead to decreased cellular functioning.

Although free radicals have traditionally been considered purely a threat to cells, such one-sided thinking is beginning to be challenged. There is increasing evidence to suggest that free radicals play an important role in modulating redox-sensitive signaling pathways on the way to muscular adaptations[40]. Results from several recent studies on animals as well as some involving athletes present the framework for a functional role of

其维生素A原功能外，β-胡萝卜素还被认为具有抗氧化特性[49]，并可能对免疫系统有积极影响[50]，且有抗癌作用[51]。维生素C是一种抗氧化剂，是人类一系列基本代谢反应（包括胶原合成）的辅助因子[52]。除了人类，这种水溶性维生素几乎在所有生物中都是内源性的。抗坏血酸的离子形式L-抗坏血酸是一种强还原剂，其氧化形式被酶和谷胱甘肽还原。维生素E是指包括生育酚和生育三烯酚的一组脂溶性化合物。α-生育酚是最具生物活性的形式，已被证明可以保护细胞免受脂质过氧化[53-54]，并预防与氧化应激相关的慢性疾病[51,55]。其氧化形式可被其他抗氧化剂如维生素C、视黄醇、泛醇、谷胱甘肽、半胱氨酸和α-硫辛酸循环回活性形式[56]。

非酶促抗氧化剂还包括辅酶Q10、多酚、α-硫辛酸和N-乙酰半胱氨酸。辅酶Q10也称为泛醌，是一种脂溶性维生素样物质，存在于大多数真核细胞中，主要存在于线粒体中[57]。它是电子传递链的一个组成部分，在细胞的能量产生中起着一定的作用。其还原形式泛醇，是体内重要的抗氧化剂。多酚是一组水溶性植物源物质，其特征是有一个以上的酚基[58]。对于已经鉴定出的几千种多酚，可以根据它们的结构和复杂性分成不同的类型，即黄酮类、木脂素类、芪类、香豆素类和单宁类。黄酮类化合物是最大的一类酚类化合物。水果和蔬菜中有丰富的多酚。例如，红葡萄酒含有多种多酚类化合物，已被证明具有治疗慢性疾病的药理学特性[59-60]。α-硫辛酸是由辛酸衍生而来的有机硫化合物。它是4种线粒体酶复合物的重要辅助因子，因此，它是有氧代谢的关键。α-硫辛酸可能具有强大的抗氧化潜力，可以循环利用维生素E[61]；然而，它在组织中的积累是有限的。N-乙酰半胱氨酸是内源性合成的抗氧化剂谷胱甘肽的副产物，它是一种半胱氨酸衍生物，在谷胱甘肽维持和代谢中发挥作用。鉴于其抗氧化特性，N-乙酰半胱氨酸已被用作营养补剂[43]。

内源性和外源性抗氧化剂均可保护机体免受氧化应激的影响。更具体地说，酶和非酶抗氧化剂的协调网络存在于胞内和胞外，从而在自由基损伤蛋白质、脂质或DNA之前清除自由基。酶抗氧化剂是细胞蛋白质，可以催化去除活性物质从而防止氧化应激。非酶促抗氧化剂，如食物中所含的谷胱甘肽或抗氧化剂，可通过催化反应以外的方式消除自由基。为了最大程度免受自由基介导的损伤，酶促和非酶促抗氧化剂有策略地在整个细胞中将细胞区室化（例如，细胞器vs.膜vs.胞质溶胶）[4]。抗氧化剂和氧化剂（即自由基）之间的平衡通常被称为“氧化还原平

reactive species, including O_2^-, H_2O_2, and NO·, as important cell signals. Activation of the mitogen-activated protein kinase signaling pathway after aerobic endurance training enhances mitochondrial biogenesis and capillarization (angiogenesis), muscle hypertrophy, and glucose transport ability[19,41]. It has been found that these adaptations to training may be dependent on changes to cellular redox potentials caused by free radicals[40] or the transient appearance of O_2^-[17-18], as these appear to stimulate the upregulation of certain important transcription factors within this pathway.

In addition, H_2O_2 formed from O_2^- in the extracellular space acts as a vasodilator, which can optimize blood flow. NO· produced in endothelial cells by nitric oxide synthase also induces vasodilation in arteries that support the contracting muscle[42], leading to an increase in blood-flow velocity[43]. The resulting increase in shear stress in the microvasculature of muscle fibers is an important stimulus for angiogenesis in muscle [44]. Endogenous oxidant-defense is also upregulated by negative feedback from reactive oxygen species, especially O_2^-[19,45].

Free radicals may also have acute positive effects. In low concentrations, they help maintain muscle force production[40]. Furthermore, during the oxidative burst of phagocytosis, macrophages release O_2^-, H_2O_2, and NO· as part of the clearing out of damaged or dead cell material, which helps speed the repair process[46].

3 Antioxidant Defense Systems

To counter reactive species, the body is equipped with highly effective antioxidant defense systems. These include non-enzymatic, enzymatic, and dietary antioxidants. Glutathione, uric acid, lipoic acid, bilirubin, and coenzyme Q10 are examples of non-enzymatic antioxidants that originate from endogenous sources and are often by-products of cellular metabolism. Principal enzymatic antioxidants are superoxide dismutase (SOD), catalase, glutathione peroxidase (GPX) and glutathione reductase, while most known examples of dietary antioxidants are tocopherols (vitamin E), ascorbic acid (vitamin C) and carotenoids (b-carotene). In addition, various polyphenolic compounds have recently been promoted as nutrient antioxidants. α-Lipoic acid and pharmaceuticals such as N-acetylcysteine and allopurinol have also been evaluated in studies that involve antioxi-

衡”，如图 1 所示。氧化应激是抗氧化剂和氧化剂失衡的结果；这发生在自由基的产生超过抗氧化能力时。相反，当抗氧化能力大大超过自由基产生速率时，就会发生还原性应激。

图 1 自由基与抗氧化剂的关系

Figure 1 Relationship between Radicals and Antioxidants

4 运动导致的氧化应激

在收缩过程中，骨骼肌是活性物质的主要来源，也是其主要靶标之一[4]。运动使摄氧量（VO_2）比静息值高 20 倍[62]。在运动肌肉细胞的线粒体中，这意味着氧气使用量增加了 200 倍[62]。20 世纪 70 年代后期首次有了针对运动导致的氧化应激的描述，在运动的人的呼出气体中[33]和运动的大鼠的组织[63]中发现脂质过氧化产物的水平增加。1982 年 Davies 等首次提供直接证据，证明高强度运动会显著增加大鼠肌肉和肝脏自由基生成并造成线粒体膜损伤[64]。有人认为这可以同时对线粒体生物合成产生刺激作用。然而，大多数早期研究集中于氧化剂在肌肉中的破坏作用，并寻找抗氧化剂的潜在益处。

在过去的 30 年中，人们对运动相关的活性物质的来源和后果的认识有了显著提高。新出现的证据表明，肌肉收缩导致的自由基产生主要发生在肌肉的胞质溶胶中，并且其数量多少受诸如环境条件、运动强度和持续时间等因素的影响[65-66]。具体而言，骨骼肌自由基的产生随着运动强度和持续时间的增加而增加。此外，在炎热的环境中和在高海拔地区（即约 4 000 m）工作期间，收缩骨骼肌会产生更多的自由基[67-68]。因此，运动导致的肌肉自由基产生的幅度在很大程度上取决于运动条件。

虽然收缩骨骼肌会产生自由基，但运动并不总是会对骨骼肌造成氧化损伤。例如，低强度和短时间运动通常不会促进骨骼肌的氧化应激[4]。尽管如此，在中等强度到高强度下进行的长时间耐力运动往往会导致未经训练的个体的骨骼肌的氧化损伤。此外，重复性离心收缩，尤其是当运动员试图适应新的运动强度时，会使骨骼肌承受相当大的压力，可能会导致肌肉的氧化损伤[69-70]。损伤性运动也会诱发炎症反

dant supplementation.

In human skeletal muscle fibers, several endogenous enzymes and substrates work together to scavenge free radicals. SOD reduces O_2^- to H_2O_2. In the cytosol, H_2O_2 can thereafter be converted to water by glutathione peroxidase (GPX), which oxidizes glutathione (GSH), or one of several peroxiredoxins with the help of thioredoxin, or to water and molecular oxygen by catalase[26]. The dipeptides carnosine and anserine also act as antioxidants by scavenging O_2^- and $\cdot OH$[47].

Non-enzymatic antioxidants, which are not synthesized in humans, must be obtained exogenously, and include the vitamins A (b-carotene), C (ascorbic acid), and E (a-tocopherol), and these vitamins are also referred to as dietary antioxidants. These substances are able to scavenge various free radicals by proton donation. Vitamin A belongs to a group of red, orange and yellow pigments called carotenoids[48]. Others include α-carotene, β-cryptoxanthin, lycopene, lutein, and zeaxanthin. β-Carotene is the most active carotenoid; after consumption it converts to retinol, a readily usable form of vitamin A. In addition to its provitamin A function, β-carotene is believed to have antioxidant properties[49] and may positively impact the immune system[50] and exhibit anticancerogenic effects[51]. Vitamin C is an antioxidant and a co-factor in a range of essential metabolic reactions in humans including collagen synthesis[52]. This water-soluble vitamin is produced endogenously by almost all organisms except humans. L-ascorbate, an ion form of ascorbic acid, is a strong reducing agent and its oxidized form is reduced back by enzymes and glutathione. Vitamin E refers to a group of fat-soluble compounds that include tocopherols and tocotrienols. α-Tocopherol is the most biologically active form, and has been shown to protect the cells from lipid peroxidation[53-54] and to prevent chronic diseases associated with oxidative stress[51,55]. Its oxidized form can be recycled back to the active form by other antioxidants, such as vitamin C, retinol, ubiquinol, glutathione, cysteine and a-lipoic acid[56].

Non-enzymatic antioxidants also include coenzyme Q10, polyphenols, α-Lipoic acid, and N-acetylcysteine. Coenzyme Q10, also known as ubiquinone, is a fat-soluble, vitamin-like substance, present in most eukaryotic cells, primarily in mitochondria[57]. It is a component of

应，进一步增加活性物质的形成[71]。然而，这些研究往往缺乏关于受试者氧化还原状态的信息，因此未能提供证据来证明活性物质在肌肉损伤中所起到的作用。在训练有素的耐力运动员的骨骼肌中，具有适应良好的内源性抗氧化缓冲系统，可以抵抗运动引起的氧化应激[4]。因此，运动是否导致氧化应激取决于几个因素，包括运动强度、持续时间以及个体的运动训练状态。

5 活性物质和运动训练适应

细胞适应自由基数量的增加，从而更能抵抗氧化应激的不利影响[72]。然而，必须强调的是，单次运动和定期运动的效果是完全不同的。定期运动能带来许多有益的影响，身体适应氧化剂水平升高，而在单次剧烈运动时，适应性的变化是微不足道的。剧烈运动带来的调整涉及增加血管舒张以增强血流和能量转运，以及通过酶的变构活性发生动力学转变，但这些可能不足以恢复氧化剂-抗氧化剂的动态平衡[20]。内源性防御机制的长期刺激需要持续存在的生理刺激来维持一定程度的促氧化环境，并有效地使抗氧化系统超负荷[73]。在运动训练，身体适应运动导致的氧化应激，并变得更能抵抗之后的氧化应激。这是通过多种不同的机制实现的，如上调氧化还原敏感基因表达和抗氧化酶水平[10,17]，增加酶活性[14,74]，刺激蛋白质周转[75]，改善DNA修复系统[76-77]，增加线粒体生物合成[8]和增加肌肉中热休克蛋白的含量[78-79]。这些适应可以正面影响损伤后骨骼肌的重塑，并减少炎症和细胞凋亡现象[20,80-81]。

中等水平的活性物质似乎是各种生理过程所必需的，而过量的自由基产生会导致氧化损伤。这可以用激素的概念来描述，激素是一种剂量-反应关系，其中低剂量的物质是刺激性的或有益的，高剂量是抑制性的或有毒性的[82]。为了适应活性物质增加，线粒体的适应性反应也符合如此的毒物兴奋效应，因此被称为线粒体毒物兴奋效应或线粒体效应[83]。活性物质的激效作用，可能是定期运动对身体健康和运动表现有益的机制[82]。从活性物质作为骨骼肌功能内源性调节因子发挥的作用，就可见一斑。活性物质是达到最佳收缩运动效果是必需的。肌肉肌丝，如肌球蛋白和肌钙蛋白，以及肌质网中的蛋白质是对氧化还原敏感的，这使活性物质具有改变肌肉收缩的能力[84]。

基于Reid关于氧化还原状态对肌肉力量产生作用的模型，对活性物质的反应可用钟形曲线描述，如图2所示[85-86]。在基线时，低水平的自由基对疲劳

the electron transport chain and plays a part in the energy production of a cell. Its reduced form, ubiquinol, acts as an important antioxidant in the body. Polyphenols are a group of water-soluble, plant-derived substances, characterized by the presence of more than one phenolic group[58]. Several thousand polyphenols have been identified and they are divided into different groups according to their structure and complexity, i.e., flavonoids, lignans, stilbenes, coumarins and tannins. Flavonoids are the largest group of phenolic compounds. Fruits and vegetables are a particularly rich source of polyphenols. For instance, red wine contains various polyphenolic compounds, which have been shown to possess pharmacological properties in the treatment of chronic diseases[59-60]. α-Lipoic acid is an organosulfur compound derived from octanoic acid. It is an essential co-factor of the four mitochondrial enzyme complexes, therefore, is crucially involved in aerobic metabolism. α-Lipoic acid may have potent antioxidant potential and can recycle vitamin E[61]; however, its accumulation in tissues is limited. N-acetylcysteine is a by-product of an endogenously synthesized antioxidant glutathione. It is a cysteine derivative and plays a role in glutathione maintenance and metabolism. Given its antioxidant property, N-acetylcysteine has been used as a nutritional supplement[43].

The body is protected against oxidative stress by both endogenous and exogenous antioxidants. More specifically, a coordinated network of enzymatic and non-enzymatic antioxidants exists in both the intracellular and extracellular locations to remove radicals before they damage proteins, lipids, or DNA. Enzymatic antioxidants are cellular proteins that catalytically remove reactive species to protect against oxidative stress. Non-enzymatic antioxidants, such as glutathione or antioxidants contained in food, can eliminate radicals by means other than a catalytic reaction. To provide optimal protection against radical-mediated damage, both enzymatic and non-enzymatic antioxidants are strategically compartmentalized (e.g., organelles vs. membrane vs. cytosol) throughout the cell[4]. The balance between antioxidants and oxidants (i.e., radicals) is commonly referred to as “redox balance” and is illustrated in Figure 1. Oxidative stress results from an imbalance between antioxidants and oxidants; this occurs when radi-

肌肉的收缩作用似乎不是很理想。来自 Reid 的研究数据表明，活性物质的适度增加会导致肌肉力量增加,而抗氧化剂会消耗氧化剂水平并抑制力量。在较高的自由基浓度下,这种情况被逆转,力量输出因时间和剂量的增加而减少[85-87]。

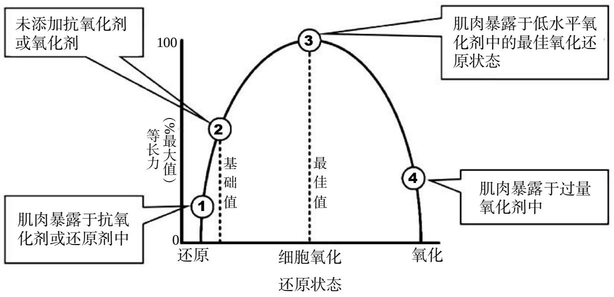

图 2 自由基对肌肉性能的影响

Figure 2 Effect of Free Radicals on Muscle Performance

6 抗氧化剂是否有益

运动员使用抗氧化剂，通常是为了防止运动引起的氧化应激的有害作用,加速肌肉功能的恢复,并提高运动能力[12-13,88-91]。目前,含有抗氧化剂的营养补剂无论在零售店还是从互联网厂商都能广泛购买。生产补充剂的公司提供的常见抗氧化剂包括维生素 E、维生素 C 和 β- 胡萝卜素。其他抗氧化产品包括葡萄提取物、白藜芦醇、叶黄素、番茄红素、硫辛酸、绿茶复合物等。研究表明,抗氧化剂的使用因地区和人群的不同而不同。尽管如此,世界各地的抗氧化剂使用率很高,一项研究报告称,约 62%的初级田径运动员使用营养补剂，其中多种维生素和矿物质是最受欢迎的[92]。

支持耐力运动员使用抗氧化剂的人认为，由于严格的运动训练导致骨骼肌损伤性自由基产生增加，抗氧化剂对保护骨骼肌纤维免受氧化损伤至关重要。这一观点得到了实验证据的支持,其证明补充维生素 C 足以钝化运动导致的自由基产生[93]。另一个支持使用抗氧化剂的论点是，许多耐力运动员的饮食缺乏抗氧化剂[94]。那些长期限制能量摄入、经常从事体重控制或减肥性运动、刻意避免摄入某些食物类别或饮食不平衡的运动员，缺乏维生素的风险最大。只有少数膳食抗氧化剂有指定的推荐每日膳食供给量(RDA)。这些抗氧化剂食物的 RDA 包括:维生素 C —男性为 90 mg,女性为 75 mg,维生素 E—15 mg,硒—55 μg。因此,对于饮食中一种或多种抗氧化剂含量较少的运动员来说，补充抗氧化剂可能对他们有益,但是,建议在开始补充治疗前咨询营养师。

反对耐力运动员使用抗氧化剂的原因有以下几

cal production exceeds the antioxidant capacity. In contrast, reductive stress occurs when the antioxidant capacity greatly exceeds the rate of radical production.

4 Exercise-Induced Oxidative Stress

During contraction, skeletal muscle is a major source of reactive species, as well as one of the main targets[4]. Exercise increases VO_2 by up to 20 times above resting values[62]. In the mitochondria of exercising muscle cells, this translates to a 200-fold greater oxygen usage[62]. Exercise induced oxidative stress was first described in the late 1970s when increased levels of lipid peroxidation products were found in the expired air of exercising humans[33] and the tissues of exercised rats[63]. In 1982, Davies et al.[64] provided the first direct evidence that high-intensity exercise significantly increased radical production in the muscles and liver of rats and caused damage to mitochondrial membranes. It was suggested that this could, at the same time, deliver a stimulus to mitochondrial biogenesis. However, the majority of early studies focused on the damaging effects of oxidants in muscle and looked for the potential benefits of antioxidants.

Over the last 30 years, an understanding of the sources and consequences of exercise-related reactive species has advanced markedly. Emerging evidence indicates that contraction-induced radical production occurs primarily in the cytosol of the muscle and the magnitude of this production is influenced by factors, such as environmental conditions and the intensity and duration of exercise [65-66]. Specifically, skeletal muscle radical production increases as a function of both the exercise intensity and duration. Moreover, contracting skeletal muscles produce more radicals during exercise in a hot environment and during work at high altitude (i.e., ~4 000 meters)[67-68]. Therefore, the magnitude of exercise-induced muscle radical production can range widely depending upon the exercise conditions.

Although contracting skeletal muscles produce radicals, exercise bouts do not always result in oxidative damage to skeletal muscles. For example, low-intensity and short-duration exercise does not generally promote oxidative stress in skeletal muscles[4]. Nonetheless, prolonged endurance exercise performed at moderate-to-high intensities often results in oxidative damage to

点。首先，没有证据表明运动导致的骨骼肌自由基对人体健康有害。定期运动可降低各种原因的死亡率，因此，运动导致的自由基增加似乎不太可能是不健康的[95]。此外，定期耐力运动训练可促进肌纤维中酶促抗氧化剂的增加，从而改善内源性保护，抵抗运动介导的氧化损伤[4]。因此，这种训练导致的内源性抗氧化剂的增加足以防止来自其他来源的氧化损伤。最后，如果耐力运动员保持营养均衡的等热量饮食，他们应该不需要饮食以外的抗氧化剂。这些考虑因素已得到该领域和美国运动医学学院专家的认可[96-97]。

也许对于耐力运动员使用抗氧化剂，最强烈的反对论点如下。首先，新的研究表明，抗氧化剂可以防止运动引起的骨骼肌适应[8,10]。令人信服的证据表明，运动导致的活性物质的产生是促进包括抗氧化酶、线粒体蛋白和热休克蛋白在内的众多骨骼肌蛋白表达的必需信号[4,65]。另一个反对运动员使用抗氧化剂的观点是，目前的许多研究都不支持抗氧化剂补充对人体健康有益的观点。例如，对68项随机抗氧化剂试验（共232 606名参与者）的荟萃分析得出结论，膳食补充β-胡萝卜素、维生素A和维生素E不能改善健康状况，并可能提高死亡率[98]。这份详细报告的结论是，维生素C和硒对人类死亡率的作用尚不清楚，需要进一步研究才能提出建议。

7 研究证据——抗氧化剂作为运动增补剂

当调查抗氧化剂在运动表现中的作用时，结果普遍不一致，大多数研究称其没有益处。20世纪70年代初，Sharman等人的研究表明补充维生素E对青少年男性游泳运动员的耐力表现没有有益的影响[99]。而且，与抗氧化剂组相比，安慰剂组在运动训练中表现出更大的心肺功能改善作用，这可能是对于补充剂不利影响的首次报道。在随后的研究中，维生素E在提高游泳运动员[100]、专业自行车运动员[101-103]、非耐力训练男子[104]、大学运动员[105]和马拉松运动员[106]的成绩方面被证明无效。此外，在对从事有氧训练的久坐老年人群的研究中，补充维生素E未能进一步提高受试者的身体机能指标[107]。辅酶Q10的补充剂对男性[108-110]的运动表现没有任何明显的影响，无论其年龄和训练状态如何。虽然有人假设多种抗氧化剂协同作用或许能更有效地对抗氧化应激，但事实上维生素E、维生素C、辅酶Q10和其他维生素和矿物质的组合未能改善竞技男子运动员[111]、自行车运动员[112-113]、铁人三项运动员[114-115]、足球运动员[116-117]、抗阻训练男子[118]、超耐力运动员[119]和中等训练男子[120]的运动表现。

skeletal muscles of untrained individuals. In addition, repetitive eccentric contractions, if unaccustomed in particular, place skeletal muscle under considerable stress that may cause muscle damage[69-70]. Damaging exercise also induces an inflammatory response, which further increases formation of reactive species[71]. However, these studies often lack the information about the subjects’ redox status and therefore fail to provide evidence for the causal role of reactive species in muscle damage. Highly-trained endurance athletes have well-adapted endogenous antioxidant buffer systems in their skeletal muscles that can resist exercise-induced oxidative stress[4]. Therefore, whether an exercise bout results in oxidative stress is dependent upon several factors, including the intensity and duration of exercise as well as the exercise training status of the individual.

5 Reactive Species and Exercise Training Adaptations

Cells adapt to increased free radicals production to become more resistant to the adverse effects of oxidative stress[72]. It has to be emphasized, however, that the effects of a single bout of exercise and regular exercise are quite different. Regular physical activity brings about numerous beneficial effects and the body adapts to elevated oxidant levels, whilst with acute exercise, the adaptation is only marginal. Acute adjustment involves increased vasodilation to enhance blood flow and fuel transport and a kinetic shift via the allosteric activity of enzymes, which may not be sufficient to restore oxidant-antioxidant homeostasis[20]. Long-term stimulation of endogenous defense mechanisms requires the continuous presence of physiological stimuli that maintain a certain degree of pro-oxidative milieu, and effectively overload the antioxidant systems [73]. With exercise training, the body adapts to exercise-induced oxidative stress and becomes more resistant to subsequent oxidative challenges. This is achieved through a number of different mechanisms, such as upregulation of redox-sensitive gene expression and antioxidant enzymes levels[10,17], an increase in enzyme activity[14,74], stimulation of protein turnover[75], improvement in DNA-repair systems[76-77], increased mitochondrial biogenesis[8], and increased muscle content of heat shock proteins[78-79]. These adaptation can positively affects remodeling of

另一方面，已有多项研究显示抗氧化剂对身体表现有积极但有限的影响。辅酶 Q10 可以提高专业越野滑雪运动员的最大摄氧量（VO_{2max}）和有氧、无氧阈，从而增加运动能力和加快恢复速度[121]。同样，在导致疲劳的运动试验期间，无论是未经训练[122-123]还是受过训练的个体[124-125]，补充辅酶 Q10 对运动表现、疲劳感觉和恢复都有有益的影响。维生素 E 补充剂也被证明对登山者在高海拔地区的表现[126]和雪橇狗的耐力表现[127]有益。在两项早期研究中，补充维生素 C 可以提高未受过训练的男性学生[128]和运动员[129]的运动能力。在 Aguilo 等人的一项研究中，补充维生素 E、维生素 C 和 β- 胡萝卜素组合后的男性运动员在最大运动试验后表现出较低的血乳酸水平，运动训练 3 个月后 VO_{2max} 较对照组增加更多[130]。

已有多项调查显示多酚具有增强运动表现的作用，包括槲皮素[31-34]、白藜芦醇[135]，以及来自葡萄提取物[136]和甜菜根汁的多酚化合物[137-140]。新的证据表明，酚类化合物的抗氧化能力应该不是其保护作用的唯一机制，其保护作用也可以是它们与细胞信号级联反应中的各种关键蛋白相互作用所介导的[141]。然而，这些发现远未达成共识，很多研究的结果是相互矛盾。例如，槲皮素补充剂已被证明对久坐的人[142-143]或骑自行车的人[144]没有增强运动表现的作用。另外还有研究发现，对于受电刺激等长收缩的小鼠，白藜芦醇不能改善它们的肌力输出和肌肉疲劳性[145]。有趣的是，在 Marshall 等人的一项研究中，维生素 C 被证明会减缓赛狗的速度[146]。

最近有人提出，在长时间亚极量运动时，N- 乙酰半胱氨酸急性给药可能会延缓人体肌肉疲劳。Medved 等人研究了 N- 乙酰半胱氨酸对未经训练的男性的肌肉疲劳和运动表现的影响。虽然 N- 乙酰半胱氨酸在高强度间歇运动中表现出可以调节血液氧化还原状态，但对于疲劳的出现时间没有影响[147]。同一研究小组也观察到，在一组混合训练和未训练但经常运动的个体中，长时间运动时，N- 乙酰半胱氨酸输液对疲劳的出现时间没有影响[148]。然而，在同一项研究中，抗氧化剂改善了血浆 K^+ 浓度的调节机制，并提出 N- 乙酰半胱氨酸的作用取决于个体的训练状态[148]。最后，据报道，长时间亚极量运动时 N- 乙酰半胱氨酸输液可延后一组训练有素的人疲劳的出现时间，这可能是通过增加肌肉半胱氨酸和谷胱甘肽的利用率而完成的[149]。摄入 N- 乙酰半胱氨酸带来的副作用是会让某些人觉得恶心。因此，对于那些在使用该补充剂时出现恶心症状的运动员，N- 乙酰半胱氨酸可能不会改善他们的耐力表

skeletal muscle after injury and attenuate inflammation and apoptosis[20,80-81].

Moderate levels of reactive species appear necessary for various physiological processes, whereas an excessive radical production can cause oxidative damage. This may be described by the concept of hormesis, a dose-response relationship in which a low dose of a substance is stimulatory or beneficial and a high dose is inhibitory or toxic[82]. The adaptive response of mitochondria to increased formation of reactive species is termed mitochondrial hormesis or mitohormesis[83]. The hormetic action of reactive species could represent a mechanism underlying the health and performance benefits of regular physical activity[82]. This can be seen in the role of reactive species as endogenous regulators of skeletal muscle function. Reactive species appear obligatory for optimal contractile activity. Muscle myofilaments, such as myosin and troponin, and proteins in the sarcoplasmic reticulum are redox-sensitive, which gives reactive species the ability to alter muscle contraction[84].

Based on Reid’s model for the role of redox state on muscle force production, responses to reactive species can be described by a bell-shaped curve as shown in Figure 2[85-86]. At baseline, low levels of free radicals appear to be suboptimal for the contraction of unfatigued muscle. The data from Reid’s studies suggest modest augmentation in reactive species causes muscle force to increase, while antioxidants deplete oxidant levels and depress force. At higher radical concentrations, this is reversed and force production decreases in a time- and dose-dependent manner[85-87].

6 Is Antioxidant Supplementation Beneficial?

It is common practice for athletes to use antioxidant supplements with the notion that they prevent the deleterious effects of exercise-induced oxidative stress, hasten recovery of muscle function, and improve performance[12-13,88-91]. At the present, nutritional supplements containing antioxidants are widely available for purchase both in retail stores and from Internet vendors. Common antioxidants offered by supplement companies include vitamin E, vitamin C and β-carotene. Many other antioxidant products exist including grape extracts, resveratrol, lutein, lycopene, alpha lipoic acid, green tea complexes and numerous others. Studies re-

现。重要的是，补充 N- 乙酰半胱氨酸对于健康的长期影响仍然未知。

抗氧化剂在运动员中的普及导致了该领域出现大量小型研究。然而，这些研究在研究设计、运动方案、人群、补充方案和分析方法等方面差异很大，这使得这个问题仍然没有定论。许多评估抗氧化剂对运动表现影响的研究质量低，受试者人数少，其中一些研究没有坚持高质量的试验要求（例如对照、双盲和随机化）。因此，将抗氧化剂作为一种有效的助剂，评估其功效时，需要谨慎。

8 研究证据——训练中使用抗氧化剂面临的干扰

最近，人们对高剂量外源性抗氧化剂如维生素 C 和维生素 E 在耐力训练中的疗效提出了疑问，一些研究表明这些抗氧化剂实际上可能会适得其反[18,20,41,111]。如前所述，人们一直认为活性氧对内源性抗氧化系统的适应以及线粒体和血管生成起着重要的信号作用。当自由基生成被过度抑制时，这些信号可能因此被削弱或消除。

对与运动相关的氧化应激升高的一种反应是通过上调强大的抗氧化酶如 SOD 和 GPX 来加强氧化剂防御。然而，抗氧化剂可能会通过干扰自由基介导的信号来阻止这种适应[17,41]。尤其是运动员参与高强度训练时，自由基的产生水平特别高。Knez 等人的研究显示，那些服用了抗氧化剂的运动员，在半铁人三项或全铁人三项运动后，其氧化损伤明显大于未服用抗氧化剂的运动员，且能量生产系统在训练过程中面临同样多的挑战，会通过增加肌纤维的线粒体质量、毛细血管密度以及改善底物的供应和利用，来增强运动能力[14]。在这里，动物和人类的对照研究也提供了强有力的证据，表明包括维生素 C 在内的口服抗氧化剂可以干扰运动导致的信号传导和随后线粒体酶细胞色素 C 的表达，线粒体酶细胞色素 C 代表线粒体体积[8]，并可以改善胰岛素敏感性[138]。此外，在参与耐力训练计划的个体中，急性补充维生素 C(1g) 和维生素 E（600 IU）似乎可防止运动引起的血管舒张[150]，后者可钝化血流带来的血管生成刺激。如果 eNOS 的 NO 释放被阻断，血管生成也可以被阻止[44,151]。在 Gomez-Cabrera 等人的研究中，对照组的人 VO_{2max} 大约是每天摄入 1 g 维生素 C 的人的两倍[8]。

另一个抗氧化剂干扰训练的例子，出现在进行剧烈运动、不习惯的运动，特别是离心运动后的肌肉损伤时。维生素 C 和维生素 E 已被证明可延缓愈合

veal that the incidence of antioxidant supplementation varies from country-to-country and across different segments of the population. Nonetheless, the use of antioxidant supplements is high around the world, as one study reported that ~62% of junior track and field athletes use nutritional supplements, with multivitamins and minerals being the most popular[92].

Supporters of antioxidant supplementation for endurance athletes reason that because rigorous exercise training results in increased damaging radical production in skeletal muscles, antioxidant supplementation is essential to protect skeletal muscle fibers against oxidative damage. This notion is supported by experimental evidence demonstrating that vitamin C supplementation sufficiently blunts exercise-induced free radical production[93]. Another argument used to support antioxidant supplementation is that many endurance athletes have diets that are deficient in antioxidants[94]. Athletes who regularly restrict energy intake, have severe weight-loss practices, eliminate certain food groups or consume unbalanced diets are at the greatest risk for vitamin deficiency. Only a handful of dietary antioxidants have a designated Recommended Dietary Allowance (RDA). The RDAs for these include: vitamin C - 90 mg for men and 75 mg for women, vitamin E - 15 mg, and selenium - 55 μg. Therefore, supplementation with an antioxidant could be beneficial for individuals who consume a diet low in one or more of these antioxidants; however, consultation with a dietitian before beginning a supplementation regimen is advised.

There are several arguments against antioxidant supplementation for endurance athletes. First, there is no evidence that exercise-induced radical production in skeletal muscle is harmful to human health. It is well established that regular exercise reduces all-cause mortality and therefore, it seems unlikely that exercise-induced radical production is unhealthy[95]. Further, regular endurance exercise training promotes increased enzymatic antioxidants in muscle fibers resulting in improved endogenous protection against exercise-mediated oxidative damage[4]. Hence, this training-induced increase in endogenous antioxidants may be adequate to protect against oxidative damage from other sources. Finally, if an endurance athlete maintains an isocaloric diet that is nutritionally well-balanced, it is likely that

和力量恢复，并在这种肌肉损伤性运动后增加氧化应激[36,152-154]。

总的来说，强势的自由基清除行为实际上会通过抑制依赖自由基的适应信号来减少训练刺激和有效性(图3)。从希望通过训练提高能力的运动员和教练员的角度来看,这些发现很有趣。难道很多人在不知不觉中通过普通的做法来抵消训练效果，比如在耐力训练后饮用富含抗氧化剂的恢复饮料或每天服用多种维生素。

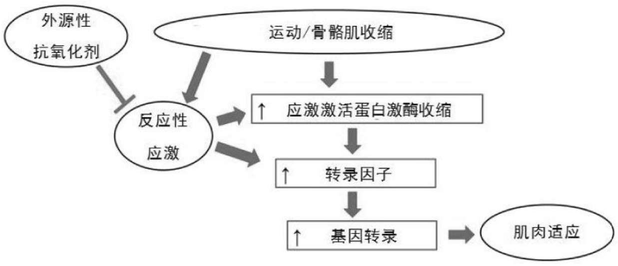

图3 目前关于运动训练中补充抗氧化剂的共识
Figure 3 Current Consensus on Antioxidant Supplementation during Exercise Training

9 实际意义和建议

关于补充剂的研究结果对营养学家、医生、从业者、运动训练师、教练和运动员以及普通人群都有重要意义。有证据表明高剂量抗氧化剂会排除运动训练的健康促进作用并干扰自由基介导的生理适应，因此在使用抗氧化剂时要谨慎。以下建议是根据当前的研究证据制定的，可以指导那些想通过服用抗氧化剂以维持健康或增强运动表现的人。

(1)经常运动的人需要优化他们的营养结构,而不是使用补充剂。

(2)他们应通过食用多种水果、蔬菜、全谷物和坚果来获得富含抗氧化剂的饮食结构。

(3)比起胶囊,全食中的抗氧化剂比例更优,而且含有众多的植物化学物质,可以协同作用,从而优化抗氧化剂的效果。

(4)抗氧化剂少量存在于食物中,因此,食用富含水果和蔬菜的饮食不太可能会导致抗氧化剂“过量”。然而，如果通过膳食补充剂摄入大量抗氧化剂,便会有更大的中毒风险或者影响健康状况。

(5)当个体有较高水平的氧化应激、能量摄入受限、从事大量减肥行为、饮食中去除了一个或多个食物群、饮食不平衡导致摄入微量营养素密度低时,可能需要补充抗氧化剂。

(6)在某些情况下,补充抗氧化剂可能是有利的，如过度训练、肌肉损伤、比赛和高海拔训练

the individual does not need supplementary antioxidants above those consumed in the diet. These considerations have been acknowledged by experts in this field and American College of Sports Medicine[96-97].

Perhaps the strongest arguments against antioxidant supplementation for endurance athletes are the following. First, new studies reveal that antioxidant supplementation can prevent exercise-induced adaptations in skeletal muscle[8,10]. Compelling evidence indicates that exercise-induced production of reactive species serves as a required signal to promote the expression of numerous skeletal muscle proteins including antioxidant enzymes, mitochondrial proteins, and heat shock proteins[4,65]. Another argument against antioxidant supplementation in athletes is that much of the current research does not support the notion that antioxidant supplementation is beneficial to human health. For example, a meta-analysis of 68 randomized antioxidant supplement trials(total of 232 606 human participants) concluded that dietary supplementation with beta-carotene, vitamin A, and vitamin E does not improve health outcomes and may increase mortality[98]. This detailed report concluded that the roles of vitamin C and selenium on human mortality are unclear and require further study before a recommendation can be rendered.

7 Research Evidence – Antioxidant Supplements as Ergogenic Aids

There has been a general inconsistency of outcomes when investigating the role of antioxidant supplementation in exercise performance with the majority of the studies reporting no benefits. In the early 1970s, Sharman et al.[99] showed that supplementation with vitamin E had no beneficial effect on endurance performance of adolescent male swimmers. Moreover, the placebo group demonstrated greater improvements of cardiorespiratory function with exercise training compared with the antioxidant group, which may be the first report of the unfavorable effect of supplementation. In the studies that followed, vitamin E proved ineffective in improving performance in swimmers[100], professional cyclists[101-103], nonresistance-trained men[104], college athletes[105], and marathon runners[106]. Furthermore, vitamin E supplements had no additive effect beyond that of aerobic training on indices of physical perfor

营,因为自由基的产生得到了强化,内源性防御被削弱。

(7)普通膳食抗氧化剂(即维生素E和维生素C)已被证明不会改善运动表现或加速运动恢复。

(8)使用抗氧化剂N-乙酰半胱氨酸治疗可改善亚极量运动时的人体运动表现。然而,N-乙酰半胱氨酸可能让某些人出现恶心症状,补充N-乙酰半胱氨酸的长期影响仍然未知。

(9)在采用抗氧化剂方案之前,需要进行仔细的产品评估,该方案应该是有临床监督的,而且这只是短期的解决方案。

10 结论

运动促进肌肉中自由基的产生，长时间/剧烈运动会导致自由基产生与肌肉抗氧化剂之间的不平衡，从而导致氧化应激。为了防止自由基介导的损伤,肌肉细胞含有内源性抗氧化剂来清除自由基。此外，从饮食中获得的外源性抗氧化剂与内源性抗氧化剂一起工作，形成一个细胞保护网络来对抗自由基介导的氧化应激。运动员是否应该使用抗氧化剂仍然是一个重要且备受争议的话题。目前,想向通过饮食摄入推荐营养素的运动员或经常运动的人推荐抗氧化剂,可以依赖的科学证据很有限。事实上,高剂量的抗氧化剂可能会妨碍运动训练对健康的促进作用,并干扰自由基介导的生理适应。抗氧化剂补充剂通常不能改善运动成绩，几乎没有证据证明它们在预防运动引起的肌肉损伤和增强恢复方面能起到作用。那些想增加抗氧化剂摄入量的人,应该考虑各种天然食品,而不是胶囊补充剂,并且应该意识到过量的抗氧化剂可能对健康和运动表现有害。

mance in a group of older sedentary adults[107]. Supplementation with coenzyme Q10 did not exhibit any significant effects on exercise performance of men[108-110]) regardless of their age and training status. Despite the presumption that antioxidants work synergistically and may therefore be more efficient in combating oxidative stress, combinations of vitamins E, C, coenzyme Q10 and other vitamins and minerals failed to improve the exercise performance of competitive male runners[111], cyclists[112-113], triathletes[114-115], soccer players[116-117], resistance-trained men[118], ultra-endurance runners[119], and moderately trained men[120].

On the other hand, there have been a number of studies showing positive but modest effects of antioxidant supplementation on physical performance. Coenzyme Q10 was associated with improved VO_{2max} and aerobic and anaerobic threshold of professional cross-country skiers that resulted in an increased exercise capacity and a faster recovery rate[121]. Similarly, supplementation with coenzyme Q10 indicated beneficial effects on performance, fatigue sensation, and recovery during fatigue-inducing exercise trials in both untrained volunteers[122-123] and trained individuals[124-125]. Vitamin E supplementation was also shown to have a beneficial effect on the performance of climbers at high altitude[126] and endurance performance of sled dogs[127]. In two early studies, supplementation with vitamin C was associated with an improved exercise capacity of untrained male students[128] and athletes[129]. In a study by Aguilo et al.[130], male athletes supplemented with a combination of vitamin E, C and β-carotene exhibited lower blood lactate levels after a maximal exercise test and a greater increase in VO_{2max} after 3 months of exercise training than the placebo group.

There have been a number of investigations showing the performance enhancing effects of polyphenols, including quercetin[31-34], resveratrol[135], and polyphenolic compounds from grape extract[136] and beetroot juice[137-140]. Emerging evidence suggests that the antioxidant potential of phenolic compounds is unlikely to be the sole mechanism responsible for their protective action, which could also be mediated by their interaction with various key proteins in the cell-signaling cascades[141]. These findings, however, are far from reaching a consensus as there are studies showing conflicting results.

For example, quercetin supplementation has been shown to have no ergogenic effects in sedentary individuals[142-143] or cyclists[144]. It was also found that resveratrol did not improve muscle force output and muscle fatigability in mice subjected to electrically stimulated isometric contractions[145]. Interestingly, in a study by Marshall et al.[146], vitamin C was shown to slow racing greyhounds.

More recently, it has been suggested that acute administration of N-acetylcysteine may delay human muscle fatigue during prolonged submaximal exercise. Medved et al.[147] have studied the effect of N-acetylcysteine on muscle fatigue and performance in untrained men. Although N-acetylcysteine was shown to modulate blood redox status during high-intensity intermittent exercise, it did not affect time to fatigue. This same research group also observed no effect of NAC infusion on time to fatigue during prolonged exercise in a group of mixed trained and untrained but physically active individuals[148]. In this same study, however, the antioxidant improved regulation of plasma K^+ concentration and it was suggested the ergogenic effect of N-acetylcysteine depends on an individual's training status[148]. Finally, N-acetylcysteine infusion during prolonged submaximal exercise was reported to augment time to fatigue in a group of well-trained individuals, possibly by increasing muscle cysteine and glutathione availability[149]. A potential side effect is that the consumption of NAC can produce nausea in some individuals. Therefore, N-acetylcysteine supplementation may not improve endurance performance in those athletes who experience nausea when using this supplement. Importantly, the long-term health effects of supplementation with N-acetylcysteine remain unknown.

The popularity of antioxidant supplements with athletes has led to a plethora of small research studies in this area. However, these studies varied considerably in terms of research design, exercise protocol, population groups, supplementation regimen and analysis methods, which made this issue still remained inconclusive. Many of the studies evaluating the effects of antioxidants on exercise performance were of low quality with small subject numbers, and some of them did not adhere to all the accepted features of a high-quality trial (e.g. placebo-controlled, double-blind, and randomization). As such, caution is needed when evaluating the efficacy of using an antioxidant supplement as an ergogenic aid.

8 Research Evidence – Interferences of Antioxidant Supplementation with Training

Recently, questions have been raised about the efficacy of high doses of exogenous antioxidants such as vitamins C and E during endurance training, with several studies suggesting that these may actually be counterproductive[18,20,41,111]. As mentioned earlier, it has been considered that reactive oxygen species play an important signaling role for adaptation of endogenous antioxidant systems and for mitochondrial genesis and angiogenesis. When radical appearance is overly suppressed, these signals may therefore be weakened or abolished.

One response to the elevated oxidative stress associated with exercise is increased oxidant defense via upregulation of powerful antioxidant enzymes like SOD and GPX. However, antioxidant supplementation may discourage such adaptations by interfering with the radical-mediated signal[17,41]. This is especially the case when athletes are involved in high-intensity training during which radical production is particularly high. Knez et al.[14] reported significantly greater oxidative damage following half or full ironman triathlons in athletes who took antioxidant supplements than in those who did not. Similarly, the challenges faced by energy production systems during training stimulate enhance exercise capacity through increased mitochondrial mass and capillary density of muscle fibers and improved provision and utilization of substrate. Here, too, placebo-controlled studies with animals and humans have provided strong evidence that oral antioxidants including vitamin C can interfere with exercise-induced signaling and subsequent expression of the mitochondrial enzyme cytochrome c, which is representative of mitochondrial volume[8], and improvements to insulin sensitivity[138]. Additionally, in humans involved in an endurance training program, acute supplementation of vitamins C (1 g) and E (600 IU) seemed to prevent exercise-induced vasodilation[150], which can blunt the blood flow-induced stimulus for angiogenesis. Angiogenesis can also be prevented if NO· release from eNOS is blocked[44,151]. In the study by Gomez-Cabrera et al.[8], mean improvement in VO2max was about twice as great in humans who received a placebo than in those who received vitamin C at 1 g·day^{-1}.

Another instance of antioxidant supplementation interfering with training is when muscle injury occurs, such as after intense, unaccustomed, and especially eccentric exercise. Vitamins C and E have been shown to delay healing and recovery of strength, and increase oxidative stress after such muscle-damaging exercise[36,152-154].

Collectively, it appears that over-dominant radical scavenging can actually reduce training stimuli and effectiveness by suppressing the radical-dependent signal for adaptation (Figure 3). Such findings are intriguing from the standpoint of athletes and coaches who wish to improve performance capacity through training. Could it be that many are unknowingly counteracting training effectiveness through ordinary practices such as consuming an antioxidant-rich recovery drink after an endurance training session or taking a daily multivitamin?

9 Practical Implications

The outcomes of supplementation studies have important implications for nutritionists, physicians, practitioners, athletic trainers, coaches, and athletes, as well as for the general population. Evidence that high doses of antioxidants preclude health-promoting effects of exercise training and interfere with radical-mediated physiological adaptations suggest caution in the use of antioxidant supplements. The following recommendations are developed based on the current research evidence and should help guide those who consider taking antioxidant supplements for maintaining health or enhancing performance:

(1) Physically active individuals need to optimize their nutrition rather than use supplements.

(2) Diets rich in antioxidants should be attained by consuming a variety of fruits, vegetables, whole grains, and nuts.

(3) Whole foods, rather than capsules, contain antioxidants presented in beneficial ratios and numerous phytochemicals that may act in synergy to optimize the effect of antioxidants.

(4) Antioxidants exist in small quantities in foods and therefore, there is limited risk of an antioxidant “overdose” by consuming a diet rich in fruits and vegetables. However, the ingestion of megadose of antioxidant via dietary supplements can increase the risk of toxicity and negative health consequences.

(5) Antioxidant supplementation may be warranted when individuals are exposed to high levels of oxidative stress, restrict their energy intake, use severe weight loss practices, eliminate one or more food groups from their diet, or consume unbalanced diets with low micronutrient density.

(6) There are certain circumstances in which antioxidant supplementation is probably advantageous, such as overtraining, muscle injury, tournaments, competitions, and high-altitude training camps, since radical production is intensified and endogenous defense weakened.

(7) It has been demonstrated that supplementation with common dietary antioxidants (i.e., vitamins E and C) does not improve exercise performance or accelerate recovery from exercise.

(8) Treatment with the antioxidant N-acetylcysteine has been shown to improve human exercise performance during submaximal exercise. However, N-acetylcysteine is associated with nausea in some individuals and the long-term effects of supplementation with N-acetylcysteine remains unknown.

(9) Careful product evaluation is required prior to adopting an antioxidant regimen, which should be clinically supervised and should only represent a short-term solution.

10 Conclusions

Exercise promotes radical production in the working muscles and prolonged/intense exercise can produce an imbalance between radical production and muscle antioxidants resulting in oxidative stress. To protect against the radical-mediated damage, muscle cells contain endogenous antioxidants to scavenge radicals. Moreover, exogenous antioxidants obtained from the diet work with endogenous antioxidants to form a supportive network of cellular protection against radical-mediated oxidative stress. The question of whether or not athletes should use antioxidant supplements remains an important and highly debated topic. At present, there is limited scientific evidence to recommend antioxidant supplements to athletes or physically active individuals who consume the recommended nutrients through diet. In fact, high doses of antioxidants may preclude health-promoting effects of exercise training and interfere with radical-mediated physiological adaptations. Antioxidant supplements generally do not improve sports performance and there is little proof to support their role in prevention of exercise-induced muscle damage and enhancement of recovery. Those who seek to augment their antioxidant intake should consider whole foods rather than capsules and should be aware of the fact that an overdose of antioxidants can be detrimental to health and performance.

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