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Cordyceps spp. as a Sports Supplement and Its Effects on Physical Performance: A Narrative Review

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Abstract

Introduction. Today's sports medicine, physical medicine, and rehabilitation are based on metabolism, energy production and use, and recovery following exertion. Cordyceps species (*C. sinensis*, *C. militaris*), rich in cordycepin, adenosine, and polysaccharides, possess unparalleled immunomodulating, anti-oxidant, and bioenergetic qualities which make them suitable for athletes as well as individuals suffering from chronic illnesses.

Research objective. In this narrative review, we discuss the scientific evidence regarding Cordyceps spp. use as a sports supplement and for therapeutic application in clinical practice with respect to aerobic performance, respiratory-metabolic parameters, fatigue biomarkers, and other more general clinical outcomes.

Methodology. A systematic search of the PubMed, Scopus, Web of Science, and NCBI databases was conducted (January–May 2026). Inclusion criteria were articles in English published from 2020 to 2026. The extracted data were processed by an overall qualitative synthesis.

Conclusions. Supplementation with Cordyceps spp. results in greater ergogenic effects through the rightward shifts of ventilatory thresholds, improved SpO₂, and enhanced mitochondrial ATP resynthesis. Bioactive compounds exhibit the up-regulation of SOD and catalase activity, reduction in MDA contents, as well as the relief of serum fatigue markers (lactic acid, BUN, CK, LDH). And it also accelerates CD34⁺/Pax7⁺ stem cells homing to muscle micro-damages, for a more rapid reduction of DOMS and it protects against sports anemia. In medical settings, Cordyceps has hypoglycemic, lipid-regulating, renoprotective, anti-cancer, and vasculoprotective effects via TLR4/MyD88/p38 and TLR4/TRAF6/NF-kappaB pathways. Nonetheless, the initiation is impeded by a certain degree of gastrointestinal tolerance, allowing for individual dosage modification and specialized supervision. Future directions should also capitalize on state-of-the-art modern bioengineering and focus on long-term RCTs.

Keywords: cordyceps, sports supplementation, aerobic capacity, post-exercise recovery, fatigue biomarkers

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Disclosure

- Funding
- Institutional Review Board Statement
- Informed Consent Statement
- Data Availability Statement
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1. Introduction

Modern sports medicine and expert performance nutrition focus on metabolic optimization and rapid recovery following exercise in athletes [22]. Although a balanced diet is the basis of dietary programming, the use of ergogenic substances as additional support for the diet has become widespread under conditions of extreme physical effort [5, 22]. These products, which come in concentrated extracts, capsules, or lyophilized tablets, are designed to promote desired physiologic adaptations and minimize post-exercise immunosuppression [3, 20, 22]. In view of the evolving landscape and the myriad legal systems governing such products, it has become imperative to confirm their efficacy through robust clinical trials [20, 22]. Indeed, numerous commonly used substances are not fully supported by scientific evidence, underscoring the need to systematically assess materials with the potential to enhance aerobic parameters, reduce oxidative stress, and protect against chronic fatigue [5, 8].

Cordyceps spp. (including *Cordyceps militaris* and *Cordyceps sinensis*), an entomopathogenic fungus traditionally used in Far Eastern medicine [12, 19]. It contains numerous biologically active components, including cordycepin, adenosine, and cordyceps polysaccharides [11, 13, 21, 24]. In recent decades, it has attracted scrutiny for its use in sports and exercise medicine and physiology for its anti-fatigue, antioxidant, immunomodulating, and hematological effects, among others [7, 8, 20, 22].

Cordyceps supplementation has been associated with enhanced exercise performance and glycogen storage in the liver and skeletal muscle and increased post-exercise recovery due to the rapid mobilization of stem cells into muscle tissue after intense exercise in clinical and athletic populations [8, 10]. Moreover, it has the ability to increase blood oxygen saturation (SpO₂) [15], increase metabolic and ventilatory thresholds [9], reduce serum levels of metabolites of fatigue post-exercise, such as lactic acid, lactate dehydrogenase, and blood urea nitrogen [8], and sustain the hematological profile by keeping anemia markers stable in distance runners [23].

What are the effects of *Cordyceps* spp.-based products on the general physical capabilities of human subjects, and how do these products affect respiratory-metabolic variables (i.e. ventilatory thresholds and oxygen saturation) and biochemical and hematological markers of fatigue in athletes [7, 15, 20, 22]?

In this narrative review, we aim to critically analyze and summarize recent scientific literature on the use of *Cordyceps* spp. in sports supplementation, focusing on aerobic performance, the kinetics of fatigue markers, and biochemical markers of recovery in athletes and active subjects [7, 20, 22]. Based on these studies in the available literature, it is suggested that the dietary supplementation with *Cordyceps* spp. induces notable ergogenic effects by improving aerobic capacity, enhancing blood oxygen transport, and accelerating post-exercise metabolism and homeostasis by reducing tissue- and serum-mediated fatigue [7, 8, 9, 15, 23].

2. Methods

Guidelines for writing this review were informed by the narrative literature review model. The collection of source materials took place between January and May 2026 across international, peer-reviewed bibliographic databases, including PubMed, Scopus, Web of Science, and NCBI. The selection of relevant literature was driven by multiple combinations of controlled terms. Primary descriptors included terms such as cordyceps, antioxidants, and supplementation in athletes. To accurately determine which reports matched the study's objective, the search terms

were refined by adding the following: *Cordyceps militaris*, *Cordyceps sinensis*, aerobic capacity, exercise performance, post-exercise recovery, fatigue biomarkers, and blood markers for anemia.

Strict chronological and language limitations were applied on the selection level — only articles published in English between 2020 and 2026 were considered. This approach enabled us to incorporate up-to-date knowledge in sports medicine, including recent research on post-exercise stem cell kinetics and red blood cell profiles in endurance athletes. The narrative nature of the report was considered, along with quality analysis and critical discussion of the biochemical pathways responsible for the ergogenic potential of *Cordyceps* spp. By its design, this structure lacks the processing of quantitative statistical data, as in meta-analyses.

3. Research results

3.1. Multidirectional Impact of *Cordyceps* spp. Supplementation on Performance, Respiratory-Metabolic Parameters, and Fatigue in Athletes

Among modern reviews on cordyceps' ergogenic effects, the direct effect on the body's physiological adaptation to extreme training loads is highlighted first [4, 15]. This supplementation profoundly alters respiratory variables, peak VO₂, and muscle cell energy metabolism, as demonstrated by mechanistically distinct clinical trials and a meta-analysis [4, 15, 22].

When examining cardiorespiratory parameters during submaximal and maximal exercise in subjects performing on a stationary bike ergometer, an upshift in metabolic thresholds has been reported after chronic consumption of standardized mycelium extracts (including the well-researched *Cordyceps sinensis* Cs-4 strain, consumed at a daily dose of ca. 1000 mg) [9]. An 8.5% increase in the ventilatory threshold (VT) and a 10.5% increase in the metabolic threshold (the point at which there is an accelerated accumulation of hydrogen ions and lactic acid in the serum) were statistically significant [4, 9]. This is a fundamental phenomenon for endurance athletes, as it enables them to perform high-intensity exercise for longer durations without reaching deep metabolic acidosis [4, 9, 15].

The breath-by-breath processing of the running tests also revealed a significant decrease in the time to reach oxygen steady state and an increase in respiratory variables [7, 9]. Runners who took *Cordyceps militaris* (in the form of an active infusion of fruiting bodies at a dose of 1 g/day for 3 weeks) showed a significant increase in peripheral blood oxygen saturation (SpO₂) while running on a treadmill and over test distances (5 km), which was directly related to an increased time to exhaustion [7].

Among the most recent and promising approaches in sports medicine is the combination of *Cordyceps sinensis* supplementation with repeated-sprint training in hypoxia (RSH) under normobaric control conditions [20]. A four-week protocol involving administration of the preparation (3 g/day) to female athletes (soccer players) working out in a low-oxygen atmosphere (FiO₂ = 14.5%) showed a synergistic adaptive effect [20]. Exposure to oxygen deficit, combined with the biochemical support of the fungal extract, led to a remarkable improvement in maximal sprinting capacity, increased peak power, and faster post-exercise recovery, all of which were superior to the effects of hypoxic training in the presence of a placebo [20].

At the biochemical and cellular levels, the main mediators of the anti-fatigue action are cordycepin (3'-deoxyadenosine) and adenosine [5, 21, 22]. These molecules have a high structural affinity for purine nucleosides and can activate mitochondrial production of adenosine triphosphate (ATP) and energy turnover via cytochrome c and AMPK-mediated enzymatic pathways [9, 13, 21]. In models of forced exhaustive physical activity, oral cordycepin treatment has been shown to significantly suppress the generation of serum indicators of tissue damage

and metabolic fatigue [21]. A rapid decrease in post-exercise levels of lactic acid and blood urea nitrogen (BUN) was observed [21]. At the same time, the enzymatic activities of serum CK and LDH are inhibited, suggesting strong protection of myocyte membranes and a concomitant decrease in mechanically induced micro-injuries to cellular structures [15, 21]. Moreover, the supplementation promotes enzymatic pathways of glycogen synthesis, resulting in overcompensation and elevated resting glycogen levels in both the liver and skeletal muscle, thereby protecting energy substrate reserves for the following training session [21, 24].

3.2. Impact on Post-Exercise Recovery Kinetics, Oxidative Stress, and Hematological Profiles

Post-exercise biological regeneration is a key determinant of the repeatability of results in high-level sports [12, 15]. In this respect, *Cordyceps* spp. has distinctive immunomodulatory and antioxidant effects that directly enhance post-exercise recovery and shield the athlete's cardiovascular system [12, 15, 16].

Redox homeostasis is disrupted during intense exercise, leading to oxidative stress and the formation of reactive oxygen species (ROS), which have detrimental effects on structural proteins and membrane lipids [8, 21]. Polysaccharide fractions and polyphenols present in *Cordyceps* act as highly efficient free-radical scavengers (an exogenous antioxidant shield) and also activate endogenous protective mechanisms [8, 11, 23]. The supplementation enhances superoxide dismutase (SOD) and catalase activities in plasma, accompanied by a short-term decrease in malondialdehyde (MDA) levels, a prominent product of lipid peroxidation [8, 21]. This reduction in oxidative stress in the hippocampus is involved in the anti-neurobehavioral effects of overtraining and protects against reduced cognitive function, working memory impairment, and central fatigue [21].

A particularly innovative discovery in the field of muscle tissue regeneration is that *Cordyceps sinensis* can regulate immune responses involved in the repair of muscle microfilaments [2]. In clinical trials in healthy men who performed damaging eccentric exercises, it has been shown that bodies preconditioned with a fungal extract exhibit enhanced post-exercise mobilization and proliferation of certain adult stem cells within injured myocytes [2]. A faster mobilization and homing of stem cells with the CD34⁺ and Pax7⁺ phenotypes to post-exercise inflammation-affected areas were observed [2]. This enhancement of the cellular response enables a significant reduction in the duration of delayed-onset muscle soreness (DOMS) and an earlier recovery of peak mechanical power-generating capacity [2, 15].

A particular problem in endurance sports (e.g., distance running, cycling) is the occurrence of so-called sports anemia (runner's anemia), which results from mechanical destruction of erythrocytes in the capillaries of the feet and from a post-exercise elevation in hepcidin levels that interferes with iron absorption [12, 16]. Clinical studies of *Cordyceps militaris* mycelium extract treatment in long-distance runners revealed a strong protective effect on the red blood cell system [16]. Regular consumption of the agent during phases of increasing training volume leads to more stable hematological indices: the normal physiological decrease in erythrocyte (RBC) count, hemoglobin mass (Hb), and hematocrit (Ht) is obviated [16]. Therefore, this ensures that the blood has optimal capacity to carry and deliver oxygen to the working muscles, preventing sudden decreases in performance due to subclinical anemia [12, 16].

3.3. General Medical Impact of Supplementation on the Human Body and Clinical Disorders

Outside sports medicine, the multi-directional biochemical nature of *Cordyceps* spp. (including cordycepic acid, D-mannitol, polysaccharides, adenosine, carotenoids and sterols) shows a wide array of proven pharmacological activities for the prophylaxis and treatment of chronic and lifestyle diseases [11, 13, 15, 17].

Metabolic Disorders: Polysaccharide fractions and cordycepin exhibited strong hypoglycemic and lipid-lowering effects [11, 13, 14]. During the development of type 2 diabetes and diabetic nephropathy, these compounds can enhance peripheral tissue insulin sensitivity, mitigate hyperlipidemia, and protect the kidney by reducing glomerular destruction and proteinuria [11, 13, 14]. Novel biotechnological strategies, e.g. *Cordyceps militaris* biomass grown on a substrate fortified with *Ginkgo biloba* seeds, show particular effectiveness in treating metabolic problems, as a synergistic enhancement of the therapeutic potential of both ingredients is experienced [14].

Immunomodulation and Oncology: Polysaccharides derived from the genus *Cordyceps* can also precisely program the immune response [11, 23]. By stimulating macrophages, T lymphocytes, and NK cells, they modulate inflammatory pathways, among others, via very selective signalling axes, i.e., the TLR4/MyD88/p38 and TLR4/TRAF6/NF-kappaB pathways [13, 23]. Conversely, cordycepin and other adenosine derivatives have direct cytostatic and pro-apoptotic effects on cell lines from several types of solid tumours (including ovarian cancer via ENT1 transporters and activation of AMPK signalling, as well as tongue cancer) [1, 13]. They suppress mRNA translation in tumorigenic cells and prevent metastasis [1, 13].

Cardiovascular System, Respiratory System, and Liver: The isolates from these mushrooms have well-established vasoprotective and pulmonary-protective effects [15, 17]. The active ingredients attenuate pathological alterations in the lung and vascular endothelium induced by long-term exposure to air pollutants, particularly particulate matter (PM_{2.5}) [17]. These compounds also inhibit NLRP3 inflammasome activation and cell pyroptosis, thereby preventing atherosclerotic plaque formation, exhibiting antihypertensive properties, and reducing the risk of ischemic attacks, such as cerebral stroke and myocardial infarction [17]. The solid-state fermentation (SSF) products also demonstrate strong hepatoprotective activity by preventing fatty degeneration of the liver parenchyma and toxic-induced hepatic injury through scavenging of chronic oxidative stress [8].

Endocrine and Reproductive Systems: Studies on extracellular polysaccharides (EPS) and mycelial fractions show that *Cordyceps* promotes reproductive function [2]. In young individuals, the use of these compounds results in significant increases in the mean area of the seminiferous tubules in the testes, total sperm concentration, and the proportion of progressively motile spermatozoa [2]. The main mechanism of action is direct stimulation of Leydig cells to produce testosterone, and therefore, it has a good potential for treatment of hypogonadism and male infertility [2, 11].

Osteoarticular System and Visual Apparatus: We found that cordycepin has phytoestrogenic activity, which supports its ability to maintain bone mineral density by suppressing bone resorption and acting as an anti-osteoporotic agent in models of menopause or ovariectomy [10]. Furthermore, it exerts a unique neuroprotective effect on the visual apparatus, protecting retinal cells against photodamage and the decline in visual function due to long-term exposure to strong light [6, 12]. Moreover, optimizing cultivation conditions for wild strains can substantially increase the production of cordycepic acid (D-mannitol), a biologically important metabolite with anti-edematous and antibacterial properties [3, 11].

4. Discussion

In total, the present body of evidence makes it clear that *Cordyceps* spp. preparations should not be considered merely as a means of inducing small transient gains in mechanical power or maximal oxygen uptake in athletes. Although enhancement of exercise parameters represents the most reported outcome in sports medicine, those obtained from RCTs and experimental models strongly support the notion that the bioactive compounds contained in this mushroom modulate a much more complex and multidirectional system of physiological interaction. This system includes post-exercise recovery kinetics, protection of red blood cell profile, attenuation of central fatigue, and immuno-metabolic modulators in patients with lifestyle diseases [4, 12, 15, 24]. This broad spectrum of action is of fundamental clinical/practical importance in the direction of homeostatic optimization in humans under the influence of either extreme physical load or pathological conditions of the body [9, 10].

One of the most important implications from the review of the literature is that multicomponent and multi-targeted intervention protocols are more likely to result in beneficial outcomes as compared with singular mono-supplementation interventions. Standardized *Cordyceps* spp. extracts administered in combination with specific training regimens, such as multiple sprints in normobaric hypoxia (RSH) or moderate-altitude endurance training, can induce more pronounced physiological adaptations [20]. Like in a clinical setting, novel biotechnological strategies taking advantage of the synergetic combination of *C. militaris* biomass with substrates like *Ginkgo biloba* seeds [6] or via solid-state fermentation (SSF) [8] present enhanced therapeutic potential in mitigating the progression of metabolic disorders in comparison to isolated fractions. This is biologically warranted, since both post-exercise fatigue and chronic disease states (for example, diabetic nephropathy, atherosclerosis) are multifactorial in origin and are driven by convergent inflammation, oxidative stress, and mitochondrial dysfunction [6, 8, 22].

Understanding the biochemical and cellular basis of the activity of *Cordyceps* spp. is critical to completely support its sale and clinical application. At the cellular level, owing to their structural analogy to purine nucleosides, cordycepin (3'-deoxyadenosine) and adenosine are able to actively participate in cellular bioenergetics by directly promoting intramitochondrial ATP resynthesis [5, 13, 22]. Simultaneously, polysaccharide moieties possess effective immunomodulating effects and finely modulate inflammatory cascades through selective signalling axes such as TLR4/MyD88/p38 and TLR4/TRAFF6/NF- κ B receptors [11, 23]. At the organism level, the consumption of extracts regularly leads to the induction of a strong antioxidant response, and systemic superoxide dismutase (SOD) activity is elevated, accompanied by diminished malondialdehyde (MDA) levels to protect membrane lipids from peroxidative damage [21, 24]. Moreover, a direct effect on the endocrine system has been proven via the stimulation of Leydig cells for testosterone production and the modulation of peripheral aromatase activity, which is extremely significant in estrogen-dependent diseases or reproductive disorders [12, 15]. These actions clearly demonstrate that the positive effects of supplementation are not random or superficial, but are instead indicative of a deep engagement with the core pathophysiological mechanisms of the body [5].

The exercise load and the biochemical status of the athlete are very tightly interwoven. Although *Cordyceps* spp. promotes the clearance of toxic metabolites (reducing levels of lactic acid and blood urea nitrogen — BUN) and maintains the integrity of myocytes (decreasing the activity of creatine kinase — CK and lactate dehydrogenase — LDH) [15, 21]. The condition of severe physical exhaustion or overexertion can hamper the absorption of nutrients and their dissemination [14]. This creates a unique treatment paradox whereby athletes at the depths of

fatigue who stand to gain the most from the biochemical support of cordycepin could have the most compromised ability to absorb and tolerate oral formulations. Thus, successful application relies not only on the pharmacological characteristics of the fungus per se, but also on a fine-tuned match of dosing timing (e.g., pretraining preparation) with the prevailing load profile and the athlete's individual capacity for adaptation [15].

In the context of tissue regeneration, particular attention should be given to the processes involved in the repair of muscle tissue. Increasing scientific results suggest that the immune preconditioning imparted by *Cordyceps sinensis* may result in more rapid mobilization and homing of stem cells (SC) of the CD34+/Pax7+ phenotype to the sites of micro-injury caused by rigorous eccentric exercise [2]. This explains why classical, isolated synthetic antioxidant-based approaches often fail or hinder training adaptation [14] when compared to the natural fungal immunomodulating approach, which speeds up recovery and reduces the length of delayed onset muscle soreness (DOMS) without blocking the natural adaptive signals of the body [2, 15].

The scope of population health and prevention of chronic diseases cannot be underestimated. Metabolic and nephrological diseases, as well as organ failure caused by environmental agents (e.g., particulate matter, PM2.5) causing overwhelming oxidative stress and NLRP3 inflammasome-dependent pyroptosis), represent the greatest challenge for modern medicine [9]. In this regard, *Cordyceps* spp. presents a promising candidate for protection. Its lipid-lowering and insulin-sensitizing activity in type 2 diabetes [6, 13], the protection of the renal parenchyma from proteinuria [6], the neuroprotective effect on ocular tissues from photodamage [13] and hippocampus from post-exercise degeneration [21] go far beyond the classic pattern of the simple "strengthening material."

Another element of high practical significance is the need to tailor protocols for dosage. From the analysis of the literature, it is not possible to identify a single best supplementation scheme for the majority of people. By contrast, an optimal approach should be highly individualized according to age, basal BMD [10], hematologic condition (e.g., to correct anemia in long-distance runners) [16], and metabolic tolerance. The principle that routine, systematic use of low amounts (e.g., 1-3 g of a standardised biomass over a minimum of 3-4 weeks) can produce more lasting adaptation in terms of stabilising blood biomarkers, oxygen saturation and maximal oxygen uptake than sporadic, large doses prompted by immediate requirements unqualifiedly underlines the significance of persistence and patience in therapy [4, 7, 15].

However, all this optimism must be balanced with a skeptical and critical appraisal of the existing evidence. Available clinical studies continue to be relatively small, of short duration, and to exhibit significant heterogeneity with respect to applied protocols and product formulations (aqueous extracts, alcoholic extracts, infusions from fruiting bodies, fermented mycelial biomass) [15, 19]. Even the endpoints are contested — some authors use mechanical power and sprinting performance only [20]; others measure subjective fatigue perception [21], and yet others use advanced hematological or biochemical (e.g., BUN, LDH, or CK parameters) [7, 16, 21]. This scattering of data limits the possibility of making direct inter-centre comparisons and formulating categorical recommendations on the absolutely optimal dosing scheme or even which strain (e.g., the superiority of *C. militaris* over *C. sinensis* in certain disease states) [10, 19].

Also interesting is the increasing attention towards new and sustainable production and delivery systems of bioactives. Cultivation parameters, ultra-high pressure extraction (UPE) method or the choice of wild strains with genetically predisposed enhanced production of cordycepic acid (D-mannitol) and other components or the production of cordycepin could bring a substantial enhancement of market possibilities and standardization of these desired agents [3, 18], and risk of contamination or high expenses allied to the collection of raw natural

material could be eliminated. These models, which constitute a promising new avenue, however, still need hard evidence for their reproducibility in industrial applications [3].

Overall, the level of evidence now available warrants inclusion of *Cordyceps* spp. supplementation within a multidisciplinary support framework in both elite sport and clinical settings. These products should not be considered to replace or substitute conventional pharmacological treatment or professional education, but as very valuable, safe and biologically justified adjunct to the dietary regimen. It can have an enormous impact on the reduction of the post-exercise and disease-related metabolic strain and on the quality of life in general, when adequately and personally applied [17, 19].

5. Conclusions

The body of evidence gathered in this study and the multi-aspect analysis of the literature allow for the formulation of the following final conclusions:

Complexity and Interdisciplinarity of Care: The modern scientific data clearly endorse the combination of specific physical activity and biomedically justified supplementation with natural source bioactive components (e.g., standardized *Cordyceps* spp. extracts) as valid and meaningful components under the umbrella of integrative care [15, 17, 19]. In this perspective, these approaches should be regarded as a complement to, and not a replacement for conventional pharmacologic therapy, a complement able to influence those aspects of symptom-, metabolism- and quality of life-domains (such as chronic fatigue, soreness or low mood) that more classical approaches are rather unable to resolve [13, 15, 21, 24].

Superiority of Multimodal and Individualized Programs: Isolated interventions based on a single manipulation have shown limited effectiveness when the goal is to enhance physical performance and exercise adaptation, and to maintain optimal systemic homeostasis [14, 15]. The maximum therapeutic and ergogenic effects are linked with the use of multimodal and highly individualized protocols involving several (i.e. aerobic, resistance, or repeated-sprint training in hypoxia — RSH) types of exercise stimuli combined with high biocomplexes, like *Cordyceps militaris* biomass grown on specialized organic matrices (e.g. *Ginkgo biloba* seeds) [6, 20]. Such integrated interventions are far more consistent with the multidimensional, complex human physiology than unidimensional interventions.

Biochemical Mechanisms of Anti-Fatigue and Cellular Protection: Cellular and molecular bases of the pleiotropic action of *Cordyceps* spp. Some active compounds, such as cordycepin and adenosine, contribute to mitochondrial ATP resynthesis [5, 13, 22], enhance peripheral blood oxygen saturation (SpO₂) [7], and modify metabolic and ventilatory thresholds [4]. At the same time, bioactive substances derived from fungi manifest a deep antioxidant activity — inducing superoxide dismutase (SOD) and reducing malondialdehyde (MDA) levels with the consequence of decreasing post-exercise damage and fatigue markers such as lactic acid, lactate dehydrogenase (LDH), creatine kinase (CK), and blood urea nitrogen (BUN) and paralleling neuroprotection of hippocampal structures [21].

Immunomodulatory, Microenvironmental, and Tissue Regeneration Modulation: A distinctive characteristic of the polysaccharide fractions from *Cordyceps* spp. is that they engage in fine immunomodulation through modulation of several critical signalling pathways, including the TLR4/MyD88/p38 and TLR4/TRAF6/NF- κ B pathways [11, 23]. Besides, *Cordyceps sinensis* supplementation remodels biological regeneration by a regulated stimulation of immunological machinery necessary for tissue repair that leads to a sped-up mobilization and

homing of stem cells with CD34+/Pax7+ phenotype into post-exercise muscle micro-injuries [2]. In addition, they also protect the hematologic profile from the effects of sports anemia [16], prevent the pathophysiological alterations provoked by environmental agents (like particulate matter PM2.5) [9], display anti-osteoporotic activity [10], and even protect the ocular system from photodamage and vision function loss [13].

Real Practical Barriers and the Necessity of Supervision: Despite its demonstrated potential, the application of habitual physical activity and sophisticated supplementation protocols in the real world is subject to substantial practical limitations. Severe fatigue, overtraining, homeostatic disturbances, and individual gastrointestinal tolerance and nutrient bioavailability under the extreme fatigue conditions are some of the most commonly reported impediments that may neutralize the impact of even the best-designed strategies [14, 15]. These barriers are not a marginal problem — they represent a significant cause of failure in therapy, and imply that any exercise and supplementation intervention must be accompanied by careful patient education, close professional specialist supervision, and meticulously individualized dosing [15].

Biotechnological Perspectives and the Need for Standardization: One last major obstacle is a unified and standardized procedure, as well as consistency of the raw materials (extracts, fermented biomass, infusions) with the same lot/batch analysis [15, 19]. In order to secure the replication of clinical results and the higher content of the required metabolites (e.g. cordycepic acid/D-mannitol and cordycepin), research in the future should be based on current bioengineering techniques. Potential pathways include modification of cultivation parameters for wild strains [3, 18], solid-state fermentation (SSF) [8], ultra-high pressure extraction (UPE) [3], and breeding of high-yield laboratory strains by the genetic basis of cordycepin synthesis [3, 18]. To conclude, it is of utmost importance that future clinical trials be led in the long term, with high statistical power, and with a harmonized set of outcome measures [15, 19].

To summarize, tailored physical exercise intervention with biomedically justified and controlled support with *Cordyceps* spp. preparations is a new promising paradigm in interdisciplinary care toward down modulation of pathophysiological strain, which at the same time optimizes metabolic and cardiorespiratory functions and in its core significantly advances quality of life of both patients and athletes [4, 7, 12, 15, 17, 19].

Disclosure

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The authors declare no conflict of interest.

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