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REVIEW ARTICLE

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Major clinical outcomes of nutrology management and the endocannabinoid system in the performance of paralympic athletes: a systematic review

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Abstract

Introduction: In the Paralympic sports scenario, recent research suggests that the connection between nutrients and the intestinal microbiota may play an important role in athlete health and performance. Exercise-induced extracellular vesicles (exosomes and microRNAs) have emerged as potential mediators of muscle crosstalk. Furthermore, clinical studies suggest that cannabidiol (CBD) may be useful for athletes due to its anti-inflammatory, analgesic, anxiolytic, and neuroprotective properties and its influence on the sleep-wake cycle. As a corollary of this, a series of implications of cannabidiol in gene expression processes modulated by microRNAs are being evidenced, impacting the immune and inflammatory systems in athletes. **Objective:** This study aimed to present the main clinical outcomes of nutritional management and the endocannabinoid system in the performance of Paralympic athletes through a systematic review. **Methods:** The systematic review rules of the PRISMA Platform were followed. The search was realized from June to July 2024 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** 135 articles were found. A total of 28 articles were evaluated and 25 were included in this systematic review. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 18 studies with a high

risk of bias and 25 studies that did not meet GRADE and AMSTAR-2. Most of the studies presented homogeneity in their results, with X^2 = 87.5% >50%. It was concluded that Paralympic athletes should feed, train, and utilize the entire supraorganism, including the intestinal microbiota, implementing gut-centered dietary strategies to achieve optimal performance. Current evidence suggests that the gut microbiota may contribute to sports performance through the production of nutritional metabolites (short-chain fatty acids, secondary bile acids), influence on gastrointestinal physiology (nutrient absorption), and immune modulation (inhibition of pathogens). Intake of adequate dietary fiber, a variety of protein sources, and emphasis on unsaturated fats, especially ω-3 fatty acids, as well as supplementation with pre-, pro-, and synbiotics, have shown promising results in optimizing the health of Paralympic athletes and with potential beneficial effects on performance. Furthermore, there is preliminary evidence supporting the anti-inflammatory, neuroprotective, analgesic, and anxiolytic actions of cannabidiol and the possibility that it may protect against gastrointestinal damage associated with inflammation and promote the healing of traumatic skeletal injuries. A specific repertoire of microRNAs regulated by cannabinoids in resting (vigilant) and lipopolysaccharide-activated microglia has been identified. The modulated microRNAs and their target genes are controlled by TLR, Nrf2, and Notch cross-talk and are involved in immune response, cell cycle regulation, cellular stress, and redox homeostasis.

Keywords: Sports nutrology. Cannabidiol. MicroRNAs. Exosomes. Metabolism. Paralympic athletes.

Introduction

In the sports nutrition field, between 40% and 100% of athletes typically use supplements, depending on the type of sport, level of competition, and definition of supplements. Nutrition helps to recover from the negative impact of an exercise-induced injury **[1]**. The outcomes of an exercise-induced injury can vary widely, depending on the nature and severity of the injury. Injuries typically result in cessation or at least reduction, of participation in sports and decreased physical activity. Following an injury, an inflammatory response is initiated, and although excess inflammation can be detrimental, given the importance of the inflammatory process for wound healing, attempting to drastically reduce inflammation may not be optimal for optimal recovery **[1-3]**.

A global effort is underway to increase physical activity and participation in sports, especially for people with disabilities, as there are implications as an effective means of rehabilitation and social inclusion **[4-6]**. In recent decades, sports for people with disabilities have evolved into competitive sports. The Paralympic Games are an international event of sporting excellence for athletes with a variety of disabilities, including mobility impairments such as amputees, spinal cord injury and cerebral palsy, visual impairments, and intellectual disabilities **[1,2]**.

Para-athletes potentially have a variety of dietary challenges, which depend on the individual characteristics of the disability. There are few reports available on the dietary intake patterns of para-athletes. The reasons for the lack of research on the dietary practices of paraathletes are that there are no general nutritional guidelines for para-athletes, para-athletes are not easily grouped by body composition using standard assessment tools such as BMI, and the physical conditions with various types of disabilities (e.g. spinal cord injury, upper or lower body amputees, cerebral palsy, etc.) affect the assessment of energy expenditure, as well as the assistive equipment used by para-athletes can affect the lifestyle of para-athletes **[1-3]**.

As an example, some studies have reported suboptimal dietary intakes in para-athletes, which may result in low iron and vitamin D levels, and wheelchair basketball players have shown inadequate energy intakes, but a high percentage of this is provided by fat (~44%), and intakes of vitamin B1, folic acid, magnesium, iron, fiber, and fluids are insufficient. Furthermore, for para-athletes, the amount of food consumed may be restricted to avoid problems with excretion difficulties **[7]**.

In light of this, nutrition generally makes a small but potentially valuable contribution to successful performance in elite athletes, and dietary supplements may make a minor contribution to this nutritional program. However, the use of supplements is widespread at all levels of sport. Products described as supplements target different issues, including managing micronutrient deficiencies, providing convenient forms of energy and macronutrients, and providing direct performance benefits or indirect benefits such as supporting intense training regimes. The appropriate use of some supplements may benefit the athlete, but others may harm the athlete's health, performance and/or livelihood and reputation, such as violating anti-doping rules, especially with the use of cannabinoids (prohibited by the World Anti-Doping Agency (WADA)), except for the use of cannabidiol **[7]**.

In this regard, cannabidiol (CBD) has shown anxiolytic, antipsychotic, neuroprotective, anti-inflammatory, and antiemetic effects **[8-10]**.

However, growing interest in the substance as medicine was renewed in the 1990s, with the discovery of cannabinoid receptors 1 and 2 (CB1 and CB2, respectively), endogenous ligands (endocannabinoids, N-arachidonoyl-ethanolamine (anandamide/AEA) and 2-arachidonoyl-glycerol (2-AG)) and enzymes as part of the endocannabinoid system (ECS) in the brain. In addition, a series of implications in epigenetic processes have also been demonstrated, through the alteration in the expression of microRNAs responsible for the modulation of the immune and inflammatory systems **[11,12]**. In this context, recent progress has been made concerning the intestinal microbiota, regenerative nutrition, and skeletal muscle metabolism. In this context, regular physical training combined with nutritional health has broad benefits for the health of the intestinal microbiota, positively acting on almost all organ systems of the body **[13-15]**. MicroRNAs (miRs) have emerged as critical regulators of numerous biological processes, modulating gene expression at the post-transcriptional level. The discovery of miRNAs as novel and important regulators of gene expression has expanded the biological understanding of the regulatory mechanism in muscle **[16]**.

In addition, adult stem cells (ASCs) stand out, such as intestinal stem cells at the base (crypts) of the intestine and muscle stem cells outside the sarcolemma next to the basement membrane of the muscle **[13]**. The tissue niche is also capable of influencing ASCs metabolism. The metabolism of tissue stem cells has focused on central carbon metabolism, that is, the generation of metabolic building blocks via glycolysis, oxidative phosphorylation, or the pentose phosphate pathway. In this sense, ASCs mediates the homeostasis and regeneration of tissues and organs, making decisions about whether to remain quiescent, proliferate, or differentiate into mature cell types. These decisions are directly integrated with the energy balance and nutritional status of the organism. Metabolic byproducts and substrates that regulate epigenetic and signaling pathways are considered to have an instructive, rather than observer, function in regulating cell fate decisions **[13]**.

Therefore, the present study presented the main clinical outcomes of nutrological management and the endocannabinoid system in the performance of Paralympic athletes through a systematic review.

Methods

Study Design

This study followed the international systematic review model, following the PRISMA (preferred reporting items for systematic reviews and meta-analysis) rules. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 06/23/2024. The AMSTAR-2 (Assessing the methodological quality of systematic reviews) methodological quality standards were also followed. Available at: https://amstar.ca/. Accessed on: 06/23/2024.

Data Sources and Search Strategy

The literature search process was carried out from June to July 2024 and developed based on Web of Science, Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, covering scientific articles from various periods to the present day. The following descriptors (MeSH Terms) were used: "Sports nutrology. Cannabidiol. MicroRNAs. Exosomes. Metabolism. Paralympic athletes", and using the Boolean "and" between MeSH terms and "or" between historical findings.

Study Quality and Risk of Bias

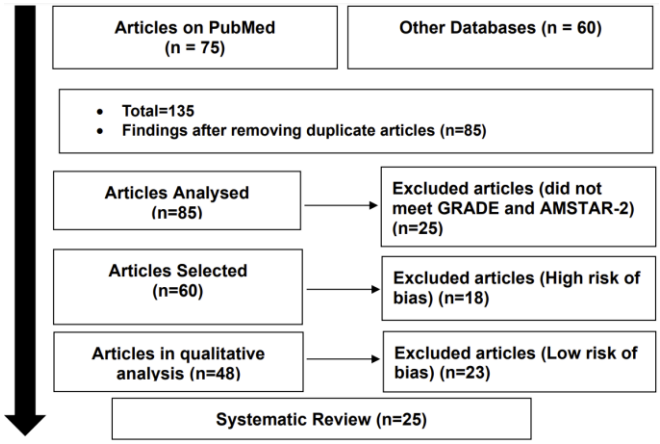
Quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident emphasis was on systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. Low quality of evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument by analyzing the Funnel Plot graph (Sample size versus Effect size), using Cohen's d test.

Results and Discussion

Summary of Findings

A total of 135 articles were found that were submitted to eligibility analysis, and 25 final studies were selected to compose the results of this systematic review. The studies listed were of medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analysis, consensus, randomized clinical, prospective, and observational. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies presented homogeneity in their results, with X^2=87.5%>50%. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 31 studies with a high risk of bias and 22 studies that did not meet GRADE and AMSTAR-2.

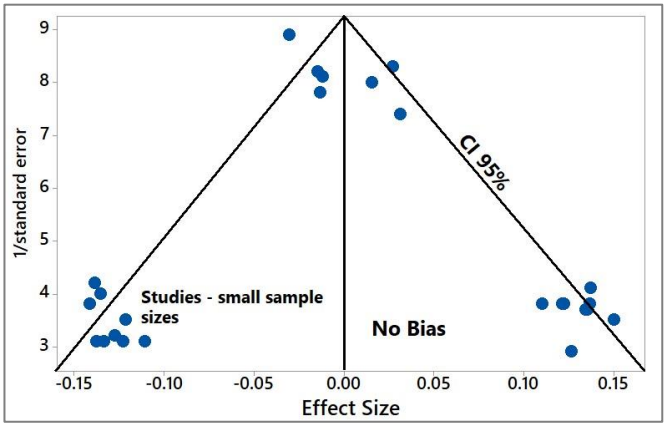
Figure 1. Selection of articles by exclusion based on GRADE and AMSTAR-2.



Source: Own Authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's Test (d). Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph had a symmetrical behavior, not suggesting a significant risk of bias, both among studies with small sample sizes (lower precision) at the bottom of the graph and in studies with large sample sizes at the top.

Figure 2. The symmetrical funnel plot suggests no risk of bias among the studies with small sample sizes, which are shown at the bottom of the graph. High confidence and high recommendation studies are shown above the graph (n=25 studies).



Source: Own Authorship.

Major Outcomes and Clinical Approaches

The demands of high-performance sports are exacerbated during the preparation for Paralympic athletes. A study examined the challenges faced and strategies used by athletes (n=7) and coaches (n=5) preparing for the Paralympic Games. The thematic analysis highlighted challenges specific to participants' sport (e.g. budget constraints, decentralized experiences, athletes with multiple disabilities), personal lives (e.g. moving to another city to access training, postponing vocational/educational developments, isolating from social circles), and associated uncertainties (e.g. COVID-19, qualifications, accreditations). Trust and communication between athletes and coaches were essential for coaches to better understand how athletes' disabilities interact with their training and competition environments and to tailor support to each athlete's unique needs. Finally, participants reflected on the "pressure" of the Games due to their performance having an impact on their "post-Tokyo" career trajectory, with some athletes contemplating retirement and others realizing the consequences of their performance on their sport-related vocation and sponsorship. Coaches also accepted that the success of their programs and job security will depend on their results at the Games **[17]**.

Authors Schneider, Sasaki, and da Costa (2023) **[18]** through a cross-sectional observational study compared two specific diet quality indices, the Brazilian Healthy Eating Index Revised (BHEI-R) and the Global Diet Quality Score (GDQS), among Brazilian para-athletes. This comparison was performed using the baseline 24-hour recall (Rec1) or an assessment of habitual dietary intake. In addition, the study explored the association of these indices with sociodemographic and behavioral sports variables. A total of 101 athletes with disabilities were included, including 23 international-level participants and 78 regional/national-level participants, with a distribution of 82 men and 19 women in 13 Paralympic sports. The comparison between Rec1 and the assessment of habitual dietary intake revealed the following median values (IQR): for BHEI-R, they were 60.3 ± 11.1 and 80.7 ± 6.2, respectively; for GDQS, they were 19.5 ± 6.5 and 18.3 ± 2.6, respectively. Most athletes had diets classified as "in need of modification" (according to BHEI-R) or "moderate risk" (according to GDQS). The comparison between sport type (team/individual), age, sex, income, education, sports scholarship, and nutritional support among diet quality indices is presented. Athletes involved in individual sports exhibited higher scores than team sports for the BHEI-R ($p<0.02$), and athletes who received nutritional support achieved higher scores on both indices ($p<0.03$). Analysis of diet quality using the initial Rec1 with the BHEI-R was considered sufficient to assess the diet quality of these athletes.

The authors Bauermann et al. (2022) **[19]** conducted a systematic review study to identify nutritional interventions and supplements that improve the performance of wheelchair athletes. Intervention

trials involving high-performance wheelchair athletes were analyzed, including those that comprised a nutritional intervention, defined as any intervention related to food, beverages, and supplementation aimed at evaluating the performance of wheelchair athletes. Of the included studies, four evaluated caffeine supplementation, of which one also evaluated sodium citrate supplementation; two studies evaluated vitamin D supplementation; one study evaluated creatine monohydrate supplementation; and one evaluated carbohydrate supplementation. Most studies were conducted in athletes with spinal cord injuries. Athletes who consumed caffeine showed improved performance.

Also, Deguchi et al. (2021) **[20]** analyzed the dietary practices of para-athletes and classified the factors (i.e., dietary perception, nutritional knowledge, and body image) that may hinder their dietary practices, and explored the practical challenges in nutritional support and improvement of nutritional knowledge for para-athletes. A total of 32 Japanese para-athletes (22 males) and 45 able-bodied university athletes (27 males) participated in the online survey. Para-athletes who responded that they knew their ideal amount and way of eating had significantly higher body image scores ($r = 0.604$, $p < 0.001$). However, the mean score for nutritional knowledge of para-athletes was significantly lower than that of university athletes (19.4 ± 6.8 vs. 24.2 ± 6.1 points, $p = 0.001$). Neither group identified a nutritionist as a source of nutritional information or as a recipient of their nutritional advice. The results indicate that para-athletes have unique dietary perceptions and inadequate nutritional knowledge.

In addition, a study by the authors Joaquim et al. (2019) **[21]** evaluated the quality of the diet of sprinters from the Brazilian Paralympic track and field team and its variation between days. All sprinters (n=28) were invited, and 20 (13 men and seven women) accepted the invitation, 13 of whom were visually impaired, four with cerebral palsy, and three with limb disabilities. Food intake was recorded by photographic records on four consecutive days, and diet quality was determined using a revised version of the Healthy Eating Index for the Brazilian population. Physical activity was assessed using an accelerometer, and metabolic unit information was used to classify exercise intensity. The results revealed that the revised version of the Healthy Eating Index score was rated as "needs modification" for all athletes. The maximum score for the components "Whole fruits", "Total vegetables" and "Dark green and orange vegetables and legumes" was achieved by 23.1% and 14.3%, 7.7% and 14.3% and 46.2% and 57.8% of males and females athletes, respectively. Only 38.5% of male athletes achieved the maximum score for the component "Total cereals". Female athletes achieved higher scores than male athletes for the component "Milk and dairy products". In this aspect of inadequate nutrition of para-athletes, it is highlighted that severe inflammation and impaired myogenic differentiation are the main obstacles to skeletal muscle healing after injury. MicroRNAs (miRs) play an important role as regulatory molecules during the muscle healing process, but the detailed mechanism of miR-mediated intercellular communication between myoblasts and macrophages remains unclear. It is known that myoblasts secrete miR-enriched exosomes in the inflammatory environment, through which miR-224 is transferred to macrophages to inhibit M2 polarization. Further data demonstrate that WNT-9a may be a direct target of miR-224 for macrophage polarization. In turn, the secretome of M1 macrophages impairs myogenic differentiation and promotes proliferation. The elevation of exosome-derived miR-224 is caused by the activation of the key factor E2F1 in myoblasts and demonstrates the RB/E2F1/miR-224/WNT-9a axis.

Besides, *in vivo*, results have shown that treatment with antagomir-224 or liposomes containing miR-224 inhibitors suppresses fibrosis and improves muscle recovery **[22]**. In addition, the transforming growth factor-β (TGF-β)/Smad pathway has been found to play an important role in inhibiting myogenesis, a key stage in skeletal muscle regeneration. MicroRNA-122-5p (miR-122) has also been shown to negatively regulate the TGF-β/Smad pathway. miR-122 may also be involved in the process of skeletal muscle myogenesis through the regulation of the TGF-β/Smad pathway. In this regard, a study investigated the impact of miR-122 on skeletal muscle myogenesis and explored its underlying mechanism. The results showed that miR-122 and myogenic markers were downregulated in C2C12 cells after TGF-β stimulation, and miR-122 overexpression could restore myogenesis inhibited by TGF-β. Furthermore, it was found that the effect of miR-122 overexpression could be rescued by TGFBR2 overexpression **[23]**.

A study evaluated the impact of different exercise modalities on the plasma concentration of miRNA-126, as a marker of endothelial damage. The plasma concentration of miRNA-126 and miRNA-133 (a marker of muscle damage) was assessed by qRT-PCR analysis in plasma samples from healthy individuals performing one of the following exercise tests: (1) symptom-limited maximal exercise test, (2) 4-h cycling, (3) marathon running, and (4) endurance exercise. A symptom-limited maximal exercise test resulted in a significant increase in circulating miRNA-126 at maximal power (2.1-fold versus baseline), while miRNA-133 concentration remained unchanged. In line with this, 4 h of cycling increased the plasma concentration of miRNA-126 with

a maximum of 30 min after baseline (4.6-fold versus baseline) with no impact on miRNA-133 concentration. Finishing a marathon increased miRNA-126 and miRNA-133. In contrast, eccentric resistance training led to an isolated increase in miRNA-133 level (2.1-fold versus baseline) with unchanged miRNA-126 **[24]**. Evidence suggests that adipose mesenchymal stem cell-derived exosome (AMSC-EXO) exhibits similar functions to AMSC with low immunogenicity and no tumorigenesis. In this regard, the composition of exosomes differs based on their sources. In addition, exosomes contain noncoding RNAs or fragments, including overlapping RNA transcripts, protein-coding region, structural RNAs, transfer RNA fragments, YRNAs, short hairpin RNAs, small interfering RNAs (siRNAs), microRNA (miRNA), messenger RNA (mRNA), and DNA. Regarding miRNA, exosomes present miR-1, miR-15, miR-16, miR-17, miR-18, miR-181 and miR-375. In addition, several cytokines, such as Tumor Necrosis Factor-α (TNF-α), Granulocyte Macrophage Colony Stimulating Factor (GMCSF), Interleukin (IL)-2, IL-6, IL-8, IL-10, IL-15, IL-1β, are expressed in exosomes **[11,12]**.

In this context, a study found that isolated quiescent muscle stem cells express fatty acid oxidation enzymes/transporters, however, as they exit quiescence and enter the cell cycle for proliferation, a metabolic transition occurs to favor glycolysis **[13]**. In this sense, SIRT1 is a target of increased glycolysis. SIRT1 represses the expression of skeletal muscle-specific maturity genes, as well as genes involved in mitochondrial biogenesis. Advanced glycolysis depletes NAD+, an essential metabolic cofactor of SIRT1, reducing SIRT1 activity and promoting downstream activation of these mature muscle-specific genes and differentiation **[13]**.

In this important metabolic and nutritional scenario of para-athletes, one of the systems that has been intensively studied in recent years is the endocannabinoid signaling pathway, since a series of important interactions of cannabinoid receptors with biochemical pathways have been clarified. In addition, a series of important implications in inflammation and the immune system that are induced by the activity of cannabinoid receptors stimulated by delta-9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD) have been observed. One of the most important is the ability to reduce the biosynthesis of pro-inflammatory mediators and the modulation of immune mechanisms. Different studies have reported that cannabinoids can reduce oxidative stress at the mitochondrial and cellular levels. There are important mechanisms modulated by the endocannabinoid signaling pathway as well as molecular and cellular links **[25]**.

Recent studies have shown the involvement of specific endocannabinoid receptors, such as the CB1 and CB2 endocannabinoid receptors, as well as their connection with important processes in sepsis, such as immune response, inflammatory response, and redox activity. In addition, a series of implications in epigenetic processes have also been demonstrated, through changes in the expression of microRNAs that are responsible for modulating the immune and inflammatory systems **[26]**. In this sense, by stimulating the CB1 and CB2 receptors through cannabinoids, such as delta-9-tetrahydrocannabinol (Δ9-THC) and cannabidiol (CBD), important changes occur in the main biochemical and cellular mechanisms, with effects on the inflammatory profile, immune response, metabolism, and metabolic state. Different research groups have also shown the impact of cannabinoids on the expression of microRNAs and on the mechanisms of transcription and genetic modulation of cellular processes for muscle regeneration **[26]**.

It is noteworthy that the molecular segment involved in the modulation of the immune response and the inflammatory cascade is represented by the expression of microRNAs **[13]**. The specific molecular activity of microRNAs in sepsis is complex, with numerous interactions being observed between Toll-Like Receptors (TLRs) and a series of other specific biological signals, such as nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), autophagy mechanisms, and apoptosis. The activity of TLRs is mediated in numerous cases by the expression of microRNAs, with subsequent modulation of molecular and biological mechanisms for the production of inflammatory mediators **[27]**.

Mature species are released from the cell as exosomes, apoptotic bodies, or high-density lipoproteins, becoming one of the pathways of intercellular communication, as well as a pathway for the modulation of specific biochemical and biological processes. These epigenetic mechanisms are also involved in the modulation of the cannabinoid system. Furthermore, recent studies have proven the existence of certain links between THC/CBD activity and the response of CB1 and CB2 receptors by modulating the expression of microRNAs **[22–26]**.

Authors Juknat et al. **[28]** conducted a study on the interactions between CB1 and CB2 receptors with microRNAs after activation of Δ9-THC and CBD. To simulate proinflammatory conditions, they stimulated BV-2 microglial cells with lipopolysaccharide (LPS) and subsequently analyzed the effects induced by Δ9-THC on microRNA expression. A significant increase in the expression of microRNA-21, microRNA-146a, and microRNA-155, which are closely linked to the biochemical pathways of TLRs and NF-κB, was

observed. Regarding CBD activity, they observed a decrease in the expressions of microRNA-146a and microRNA-155, as well as an increase in the expression of microRNA-34a. A similar study carried out by Yang et al. **[29]** showed a decrease in the expression of microRNA-17, microRNA-92, microRNA-421, and microRNA-374b, induced by the action of Δ9-THC.

A study evaluated the impact of two doses of CBD oil on inflammation (IL-6), performance, and pain following an eccentric loading protocol in athletes. Participants (n = 4) participated in three conditions (placebo, low dose, and high dose) in this randomized, counterbalanced design. Each condition took 72 hours to complete, with a 1-week washout period between conditions. At the beginning of each week, participants underwent a loading protocol of six sets of ten repetitions of eccentric-only biceps curls. Participants consumed placebo, low dose (2 mg/kg), or high dose (10 mg/kg) CBD oil capsules immediately after the session and continued every 12 hours for 48 hours. Venipunctures were performed before exercise and repeated 24, 48, and 72 hours post-exercise. Blood samples were centrifuged for 15 minutes in lithium heparin gel vacutainers. Plasma was separated from cells and stored at - 80° until analysis. Samples were analyzed using an IL-6 immunoassay (ELISA). There were no differences in inflammation between conditions or over time, handgrip strength between conditions or over time, or biceps curl strength between conditions or over time. There were no differences in pain between conditions, but there was a difference over time. However, there was a visible increase in IL-6 48 (4.88 ± 6.53) and 72 hours (3.12 ± 4.26) post-exercise in the placebo condition, which was not observed in the low (48: 0.35 ± 2.22; 72: 1.34 ± 5.6) and high (48: 1.34 ± 1.34; 72: -0.79 ± 5.34) dose condition **[30]**.

Finally, a study investigated the effect of cannabidiol (CBD) oil on perceived muscle soreness, inflammation, and strength performance following eccentric elbow flexor exercise (EEFE). Thirteen untrained men (mean ± SD age: 21.85 ± 2.73) performed 6 sets of 10 maximal isokinetic elbow flexor EEFE muscle actions as part of a double-blind, crossover design. Noninvasive measures (perceived pain, arm circumference, suspension joint angle (JA), and peak torque (PT)) were performed PRE, POST, 24-h, 48-h, and 72-h post- EEFE. All subjects completed the supplement (CBD: 150 mg POST, 24-h, 48-h) and placebo (PLC: POST, 24-h, 48-h) conditions separated by 2 weeks. As a result, there was no condition x time interaction or main effect of condition ($p>0.05$) for perceived pain, arm circumference, JA, or PT. There were main effects for the time of perceived pain. Thus, the current dose of 150 mg of CBD oil at POST, 24 hours and 48 hours did not affect non-invasive markers of muscle damage in the upper extremity **[31]**.

Conclusion

It was concluded that Paralympic athletes should feed, train, and utilize the entire supraorganism, including the gut microbiota, implementing gut-centered dietary strategies to achieve optimal performance. Current evidence suggests that the gut microbiota may contribute to sports performance through the production of dietary metabolites (short-chain fatty acids, secondary bile acids), influence on gastrointestinal physiology (nutrient absorption), and immune modulation (inhibition of pathogens). Intake of adequate dietary fiber, a variety of protein sources, and an emphasis on unsaturated fats, especially ω-3 fatty acids, as well as supplementation with pre-, pro-, and synbiotics, have shown promising results in optimizing the health of Paralympic athletes and with potential beneficial effects on performance. Furthermore, there is preliminary evidence supporting the anti-inflammatory, neuroprotective, analgesic, and anxiolytic actions of cannabidiol and the possibility that it may protect against inflammation-associated gastrointestinal damage and promote the healing of traumatic skeletal injuries. A specific repertoire of microRNAs that are regulated by cannabinoids in resting (vigilant) and lipopolysaccharide-activated microglia has been identified. The modulated microRNAs and their target genes are controlled by TLR, Nrf2, and Notch cross-talk and are involved in immune response, cell cycle regulation, as well as cellular stress, and redox homeostasis.

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Similarity Check

It was applied by Ithenticate®.

Peer Review Process

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