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The influence cannabidiol on delayed onset of muscle soreness

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Abstract
Introduction: Exercise induced muscle damage (EIMD) can result in a condition commonly known as delayed onset of muscle soreness (DOMS). The influence the well-known anti-inflammatory effects of cannabidiol (CBD) can have on DOMS has yet to be determined. The aim of this study was to determine the influence CBD can have on EIMD DOMS. Materials and Methods: Twenty-three trained participants completed a lower extremity EIMD protocol prior to being randomly assigned to either a CBD, MCT or null group. Self-report visual analog scale (VAS) scores were used to determine the level of soreness the participant was experiencing throughout the study (pre-, post-EIMD protocol, 24-, 48-, 72- and 96-hours post-EIMD protocol). The CBD group was given a 1ml solution of CBD and MCT oil. This solution contained 16.67mg of CBD. The MCT group received 1ml of MCT. The null group received nothing. **Results:** Each group reported significantly different post-EIMD VAS score when compared to pre-EIMD. The CBD group reported significant differences in VAS score at post-EIMD to 24-hours post-EIMD, at 48-hours post- EIMD and 72-hours post-EIMD. At 96-hours post-EIMD the CBD group reported VAS scores closer to pre-EIMD levels than either the MCT or null groups. Conclusions: CBD appears to have a significant influence on muscle soreness associated with EIMD DOMS when consumed immediately after strenuous exercise. Additionally, the rate of recovery with CBD use is greater when compared to MCT only or no intervention.

Keywords: Cannabidiol, endocannabinoid system, inflammation, pain, endocannabinoid

Introduction
Since the 1940s, a considerable number of published articles have addressed the chemistry, biochemistry, pharmacology, and clinical effects of CBD [1]. The last decade has shown a notable increase in the scientific literature on CBD, owing to its identification as being beneficial in reducing nausea and vomiting, combating psychotic disorders, decreasing inflammation, lessening anxiety, reducing depression, improving sleep, and increasing a sense of well-being [2-5]. Findings presented at the International Cannabinoid Research Society, reported that use of CBD was beneficial for treatment of inflammation, metabolic syndrome, overweight and obesity, anorexia/cachexia syndrome, and osteoarthritic and other musculoskeletal conditions [6].

Exercise induced muscle damage (EIMD) can result in a condition known as delayed onset muscle soreness (DOMS). This condition is commonly experienced by individuals who have been physically inactive for prolonged periods of time, and begin with an unexpected bout of exercise, but can also occur in athletes who exercise beyond their normal limits of training [7]. The manifestation of DOMS can also be caused by eccentric or unfamiliar forms of exercise. Clinical signs include reduced force capacities, increased painful restriction of movement, stiffness, swelling (inflammation), and dysfunction of adjacent joints. Although DOMS is considered a mild type of injury, it is one of the most common reasons for compromised sports performance [8]. The signs and symptoms of DOMS begin 6-12 hours after exercise, increase progressively until they reach peak pain at 48-72 hours post EIMD, and decrease until they disappear 5-7 days later [9]. DOMS is one of the most common recurrent forms of sports injury that can affect an individual's performance, and discourage participation in further physical activity or exercise [10].

Delayed-onset muscle soreness is a type of ultrastructural muscle injury [8]. The role of inflammation during exercise-induced muscle injury has not been clearly defined.

It is possible that the inflammatory response may be responsible for initiating, amplifying, and/or resolving skeletal muscle injury. Several modalities have been investigated in the search for a treatment that may reduce the effects of EIMD DOMS and/or accelerate recovery [10]. An element that has not been investigated is the role cannabidol (CBD) oil might have in the recovery from EIMD DOMS.

Cannabidiol (CBD) oil is a naturally occurring constituent of industrial hemp and marijuana collectively called cannabis. CBD oil is one of at least 85 cannabinoid compounds found in cannabis and is popular for its medicinal benefits. CBD is generally considered to be safe and has been used medicinally for decades. The suggested medicinal effects of CBD include decreasing anxiety, improving sleep, and providing other neuroprotective effects [11]. Cannabinoids have their effect mainly by interacting with specific receptors on cells in the brain and body: the CB1 receptor, found on neurons and glial cells in various parts of the brain, and the CB2 receptor, found mainly in the body's immune system. There is also growing evidence that CBD acts on other brain signaling systems, and that these actions may be important contributors to its therapeutic effects [12]. These therapeutic effects include, but are not limited to, a significant anti-inflammatory response [13-15]. Although studies have demonstrated the calming, anti-inflammatory, and relaxing effects of CBD on a number of conditions, research regarding the use of CBD oil to attenuate EIMD DOMS is lacking. Therefore, the purpose of this study was to determine the influence cannabidiol oil has on attenuating delayed onset of muscle soreness as a result of exercise induced muscle damage.

Materials and Methods

Twenty-three healthy participants reported to the Functional Performance Laboratory at the University of South Carolina Aiken on six different occasions (T1–T6) during the study.

All study protocols were approved by the University of South Carolina Institutional Review Board (Pro00082710). This was a blinded study in which the participant's names and group assignment were withheld from the statistician. Only until statistical analyses were completed were the results contextualized.

At T1 participants were presented with an opportunity to offer informed consent to agree to participate in this research. Following the completion of this agreement, anthropomorphic measurements (height, weight, age, sex and body composition (via BodPod, COSMED USA Inc, Concord, CA, USA) were collected. Prior to attending T1, participants were asked to refrain from eating for at least three hours. This request was an effort to remain within manufacturer guidelines for a more accurate body composition assessment.

After the participant's body composition was assessed their 1-repetition maximal (1RM) load for a barbell back squat was determined. The participants were familiar with the barbell back squat movement and had performed the movement regularly (between 1 and 3 times per week) for the past three months, per inclusion criteria. The establishment of this 1RM followed the guidelines established by the National Strength and Conditioning Association [16]. All weightlifting completed during this study was closely monitored by the research team. All participants were required to complete the weightlifting portions of this research inside a squat rack, with safety rails positioned at an appropriate level and with a trained spotter at the ready to assist the participant if the need occurred.

Following T1 the participant scheduled their T2 experience with the research team. T2 occurred 72 hours post T1 in order to offer the participant ample opportunity to recover from any effects they may have experienced as a result of completing T1.

At T2 participants indicated their perceived rating of muscle soreness by moving a marker along a 100-cm visual analogue scale (VAS). The VAS was numbered from 0 to 100 cm (on the reverse of the scale, unseen by the participant), whereby 0 cm indicated 'no muscle soreness', 50 cm signified that the muscles 'felt sore upon movement' and 100 cm that the muscles were 'too sore to move'. Muscle soreness was determined by measuring the distance of the marker to the nearest centimeter. This technique has been used in previous studies and has been shown to be reliable and valid [17].

After the participant has completed the first muscle soreness protocol in T2 participants completed the EIMD DOMS protocol. The EIMD DOMS protocol consisted of the athlete completing a self-determined warm-up followed by 4 sets of 10 repetitions of the barbell back squat movement at a load of 80% of the previously determined (T1) barbell back squat 1RM. The EIMD DOMS protocol was consistent with previously published research and has been shown to successfully inspire a condition of DOMS, while maintaining the safety of the participants [18]. Immediately following the completion of the EIMD DOMS the participant completed the muscle soreness assessment protocol a second time. Following this second muscle soreness assessment protocol the participant was randomly assigned to one of three groups: 1) CBD oil, 2) MCT or 3) No intervention.

The CBD group was administered a 1 ml dose of CBD oil containing approximately 16.67 mg of CBD. These amounts were determined by the CBD oil manufacturer, published on the CBD oil container and corresponding independent laboratory analysis offered on the manufacturer's website (purespectrumcbd.com, Pure Spectrum, Evergreen, CO, USA). The other content of the CBD solution was medium chain triglyceride (MCT) oil. The MCT group was administered a 1ml dose of MCT oil. Both the CBD and MCT oil groups were offered the respective dose in a measured dropper to ensure accuracy of dose. Research team members administer the dose. The CBD/MCT solution closely matched the MCT only solution in appearance, odor and taste.

The participants had the dose placed sublingually with the solution remaining under their tongue for 30 seconds prior to swallowing. The Null intervention group was offered nothing. This completed the T2 component to this study. Participants in either the CBD or MCT groups were not informed of the respective group in which they were assigned to maintain the strength of the research design.

Following the completion of T2, participants scheduled T3-T6 visits with the research team. T3 – T6 took place twenty-four (T3), forty-eight (T4), seventy-two (T5) and ninety-six (T6) hours post-T2. At each T3 – T6 visits, participants completed the EIMD DOMS muscle soreness assessment (VAS measure) at each visit.

Statistical Analysis

Anthropomorphic, pooled and respective group VAS data were calculated and reported in mean value with standard deviation value. Paired sample t-tests were conducted to determine whether there were statistically significant differences observed from the reported pre-EIMD state of participants and the varying time periods post-EIMD. Results from the paired sample t-tests were reported with designation of statistical significance being indicated. All statistical analysis was conducted using SPSS Statistics v 25.0.0.0.

Results

Physical characteristics of each group were not significantly different. The mean age of participants was 22.13 (± 1.38), the mean weight 78.56 kg (± 19.18) and the mean height 170.7cm (± 9.21). Consequently, Body Mass Index (BMI) did not significantly differ between groups. The amount of weight lifted for each respective group and the corresponding load based upon 80% of that maximal effort differed. The mean value of the pooled sample one repetition maximal back squat was 84.49 kg (± 36.49), while the CBD group tallied a mean maximal load of 102.84kg (± 45.15), the MCT group 82.39kg (± 34.44) and the Null group 65.91kg (± 16.23).

Table 1: Pooled and group anthropomorphic information (mean ± standard deviation)

	Pooled (N=23)	CBD Group (N=8)	MCT Group (N=8)	Null Group (N=7)
Age (yr)	22.13 ± 1.38	21.78 ± 1.63	23.27 ± 0.78	24.12 ± 1.12
Weight (kg)	78.56 ± 19.18	76.95 ± 14.36	75.22 ± 17.30	84.21 ± 26.52
Height (cm)	170.7 ± 9.21	173.13 ± 7.79	169.75 ± 13.2	169.00 ± 4.76
Body Comp (%)*	27.25 ± 12.19	24.25 ± 10.96	26.89 ± 11.79	31.10 ± 14.61
BMI**	26.04 ± 5.77	25.71 ± 3.79	25.73 ± 3.23	26.77 ± 9.59
1 RM (kg)***	84.49 ± 36.49	102.84 ± 45.15	82.39 ± 34.44	65.91 ± 16.23
% 1RM ^	67.59 ± 29.19	82.27 ± 36.12	65.91 ± 27.56	52.72 ± 12.99

* Body Composition, ** Body Mass Index, *** One Repetition Maximal Load, ^ Percentage of 1RM

The pooled and respective groups reflected similar patterns in reporting visual analog scale (VAS) of soreness throughout the study. The Pre-EIMD score was the lowest of all reported VAS scores (Pooled: 10.49 ± 12.32, CBD: 10.49 ± 12.32, MCT: 9.27 ± 7.57, Null: 5.64 ± 6.40). Post-EIMD VAS scores were the highest reported scores for both the CBD (60.03 ± 24.37) and MCT (37.99 ± 26.94) groups, while the Null group reports a VAS score of (25.50 ± 18.34). At the 24-hours post-EIMD period both the CBD and MCT groups report VAS scores lower than directly post-EIMD (39.58 ± 18.52, 32.24 ± 27.94 respectively), while the Null group reports a score higher 36.63 ± 18.35. At the 48-hour post-EIMD mark the CBD group and the MCT group report VAS scores higher than reported at the 24-hour post-EIMD period (44.83 ± 26.92, 34.76 ± 20.63), while the Null group reported a mean VAS score lower (32.00 ± 21.12) than the previous reported score. Each group reported a lower VAS score at the 72-hour post-EIMD point when compared to the 48-hour post-EIMD score (CBD: 24.37 ± 17.74, MCT: 27.70 ± 14.01, Null: 20.47 ± 20.12). VAS scores at the 96-hours post-EIMD point continued the trend of lower scores when compared to the previous reported scores (CBD: 18.29 ± 5.21, MCT: 22.04 ± 8.43, Null: 22.04 ± 8.43).

Table 2: Pooled and group visual analog scale (VAS) scores (mean± standard deviation)

	Pooled (N=23)	CBD Group (N=8)	MCT Group (N=8)	Null Group (N=7)
Pre-EIMD	10.49 ± 12.32	17.57 ± 7.91	9.27 ± 17.57	5.64 ± 6.40
Post-EIMD	41.17 ± 26.76	60.03 ± 24.37	37.99 ± 26.94	25.50 ± 18.34
24hr Post-EIMD	36.30 ± 21.05	39.58 ± 18.52	32.24 ± 27.94	36.63 ± 18.35
48hr Post-EIMD	37.54 ± 22.88	44.83 ± 26.92	34.76 ± 20.63	32.00 ± 21.12
72hr Post-EIMD	21.01 ± 16.93	24.37 ± 17.74	27.70 ± 14.01	20.47 ± 20.12
96hr Post-EIMD	14.82 ± 17.33	18.29 ± 25.21	22.04 ± 8.43	13.32 ± 13.94

Each group reported statistically significantly different scores from pre-EIMD protocol completion to post-EIMD protocol completion (CBD: p=0.013, MCT: p=0.024, Null: p=0.030). The CBD group reported statistically significant different VAS scores from post-EIMD to 24-hours post-EIMD (p=0.046) and from 48-hours post-EIMD to 72-hours post-EIMD (p=0.041).

Table 3: Results of Paired Sample t-test of VAS scores

		CBD Group	MCT Group	Null Group
		(N=8)	(N=8)	(N=7)
Pre-EIMD to Post-EIMD		0.013*	0.024*	0.030*
Post-EIMD to 24hr Post-EIMD		0.046*	0.547	0.245
24hr Post-EIMD to 48hr Post-EIMD		0.231	0.744	0.533
48hr Post-EIMD to 72hr Post-EIMD		0.041*	0.199	0.400
72hr Post-EIMD to 96hr Post-EIMD		0.533	0.068	0.099
* indicates statistically significant difference between VAS scores				

Discussion

To our knowledge this is the first research effort to determine the influence cannibidiol can have on delayed onset of muscle soreness as a result of exercise induced muscle damage. Our results indicate that consuming a CBD/MCT oil solution immediately after performing a EIMD protocol has a significant influence on the reduction in DOMS when compared to those consuming a 1ml dose of MCT oil or having no intervention.

Each group reported significantly different VAS score from pre-EIMD protocol completion to post-EIMD protocol completion. This would be expected and is an indication the protocol was effective inspiring DOMS. However, the consistency in group reporting relative to the VAS did not continue. The MCT group and the Null group did not report a statistically significant difference between any other reporting period and the previously reported score. Whereas the CBD group reported statistically significant different scores at post-

EIMD to 24 hours post-EIMD, 48 hours post-EIMD and 72 hours Post-EIMD. Both the CBD group and MCT group reported peak VAS scores immediately following EIMD protocol completion. This peak was followed by a decline in score at the 24 hour post-EIMD mark for the CBD and MCT groups. The Null groups reported a steady decline in VAS score from following the 24 hour post-EIMD reporting.

At the 48 hours, post-EIMD point, both the CBD and MCT groups reported the second highest VAS score. This is consistent with the literature in that EIMD DOMS peaks at approximately 48 hours post-exercise. This uptick in VAS scores was followed by a decline at the 72 and 96 hour post-EIMD period. It should be noted that the CBD group reported a VAS score at the 96 hour post-EIMD point closer to the pre-EIMD score than either the MCT or Null groups. This may suggest a more rapid return to pre-EIMD condition. Also, worth drawing attention to is the CBD group reported higher VAS scores than the MCT and Null groups in general. When examining the information presented in Table 1, a noticeable difference in the amount of weight achieved in the one repetition maximal load and correspondingly in the 80% of that maximal effort. This may offer some reasoning behind the elevation in reported VAS score.

DOMS is one of the most common reasons for impaired muscle performance in sports and is associated with muscle soreness, reduced muscle strength, and range of motion, and is frequently observed both in professional and recreational athletes [9]. Exercise induced muscle damage (EIMD) has been known to inspire a condition of muscle soreness know as delayed onset of muscle soreness (DOMS). DOMS usually occurs after an increase in intensity or volume of training or when the schedule of exercise is altered [19-21]. The classical symptoms of DOMS include strength losses, pain, swelling, tenderness or stiffness, loss of full range of motion, flexibility, force production and mobility. It is known that delayed onset muscle soreness increases the intensity of pain within 24 h after exercise, reaches a peak between 24 h and 48 h, disappears within 5–7 days after exercise. The results of this research effort are consistent with this information, with the CBD group reporting statistically significant reduced levels of soreness in respective 24-hour periods. This reduction in soreness may lead to an athlete being able to return to training sooner than an athlete that remains at a relatively elevated level of soreness. In this research, a 16.67mg dose of CBD in a 1ml MCT oil solution had significant statistical effect on muscle soreness. However, it is not completely understood how CBD interacts with the body to influence DOMS.

The mechanism of action of CBD is multifold [11]. These underlying mechanisms of endocannabinoid action consists of the interaction of specific cannabinoid receptors (CB1, CB2) with their endogenous ligands such as anandamide (N-arachydonyl-ethanolamine) and 2AG (2-arach- ydonyl-glycerol) [22-24]. The CB1 receptors are located mainly in the brain and modulate neurotransmitter release in a manner that (1) prevents excessive neuronal activity, thus calming and decreasing anxiety; (2) reduces pain; (3) decreases inflammation; (4) regulates movement and posture control; and (5) controls sensory perception, memory, and cognitive function [25]. There are more CB1 receptors in the brain than all the dopamine, noradrenaline and serotonin receptors combined and ten times more than opioid receptors. Anandamide and 2-AG, the natural ligands, are present in the same areas as CB1 receptors [25]. Anandamide, an endogenous ligand that occurs naturally within our bodies, binds to the CB1 receptors through the G-protein coupling system. 2-AG, the major endogenous cannabinoid of the brain [26].

CBD has an indirect effect on the CB1 receptors by stopping the enzymatic breakdown of anandamide, allowing it to stay in the system longer and to provide its medical benefits [27]. Additionally, 2-AG modulates pain receptors inhibiting both mechanical hyperalgesia and neuro-inflammation [26]. CBD has also been reported to have a mild effect on the CB2 receptors, which are in the periphery of the lymphoid tissue. The CBD helps to mediate the release of cytokines from the immune cells in a manner that helps to reduce inflammation and pain [27].

Other mechanisms of action of CBD include stimulation of vanilloid pain receptors, such as the transient receptor potential cation channel subfamily V member 1 (TRPV-1) receptor, which are known to mediate pain perception, inflammation, and body temperature. CBD may also exert its antianxiety effects by activating adenosine receptors that play a significant role in cardiovascular function, causing a broad anti-inflammatory effect throughout the body [28]. At high concentrations, CBD directly activates the 5-HT1A serotonin receptor, thereby conferring an antidepressant effect [29]. CBD has been found to be an antagonist at a potentially new third cannabinoid receptor (i.e., G protein- coupled receptor 55, or GPR55), which resides in the caudate nucleus and putamen and can contribute to osteoporosis when stimulated [30].

Considering these diverse and varied effects of CBD on the human machine it is no wonder that in the present study that CBD oil had a positive effect on muscles soreness. EIMD is designed to invite muscle soreness through inflammation resulting in pain. It is this inflammation and pain that inhibits movement post-EIMD. Numerous research studies have reported CBD having a significant influence on inflammation and pain. Additionally, it is not an uncommon response to prolonged discomfort for symptoms of anxiety and/or depression to develop, furthering the feelings of pain resultant from the EIMD. Results of research indicate that CBD has positive effects on anxiety and depressive symptoms. Lastly, CBD has influence on CB1 receptors that have been shown to effect movement and posture control. The results of our research indicated an individual can continue a normal movement pattern after an episode of EIMD sooner when ingesting CBD. This is a perfectly logical result considering the information offered above.

In concert with a substantial about of research, the role of CBD dose has yet to be determined. What is perfectly evident is that CBD has diverse utility. The amount of CBD to be used for each respective condition or desired outcome is not known and very well could have multiple confounding factors, which certainly would not be limited to the current state of inflammation the individual is in at the time of CBD ingestion, dietary history, genetic conditions, body mass, body composition or sleep patterns.

Conclusion

The results of this study indicate that CBD oil can have a significant influence on delayed onset of muscle soreness due to exercise induced muscle damage. Although the exact mechanism(s) of how delayed onset of muscle soreness is influenced by CBD has not been definitively determined, CBD oil appears to be a useful treatment for exercise induced muscle damage. CBD allows an athlete to return to a level of muscle soreness closer to that of pre-EIMD sooner than the MCT or null intervention. Further research should investigate the role CBD dose level, nutrition, sleep, type of exercise and other factors have on CBD's ability to attenuate the effects of

exercise induced muscle damage and aid in an athlete's recovery process.

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