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The Influence of Cannabidiol on Flow-Mediated Dilation in Exercising Populations: A Narrative Review

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Abstract

Cannabis and its compound constituents are being used globally for medicinal and recreational purposes. There has been a growing interest in the use of cannabis, specifically cannabidiol (CBD), and its potential effects on vascular health measures. However, no study has investigated the use of CBD vascular health measures via flow-mediated dilation (FMD) ultrasound assessment. This review aims to critically evaluate emerging evidence of the influence of CBD on vascular health via FMD ultrasound assessment in exercising populations. Examining associations among CBD use, vascular health, and exercise may enhance understanding of how cannabis constituents affect cardiovascular response during exercise. Illuminating the cardiovascular effects of CBD on exercising populations is vital for researchers and sports practitioners, given the global use of this cannabinoid and its potential to interact with exercisers' vascular health and exercise performance. While few examinations of CBD and FMD have shown effects on performance and vascular health, studies of adequate rigor to demonstrate cannabinoid effects on FMD require future research.

Key Words: *CBD, FMD, vascular health, exercise*

1 Introduction

Within the last 10 years, there have been noteworthy increases within the scientific literature on cannabidiol (CBD) research, as it has been suggested to have potential therapeutic properties aiding in inflammation, anxiety, sleep, well-being, musculoskeletal conditions, and vascular function [1,5,18,28,47]. The inflammatory potential of CBD has recently taken the spotlight within the context of exercising populations, with past and current active adults and athletes alike claiming advocacy for CBD usage without evidence-based support to encourage its efficacy [5,27-28]. Thus, the rapid influx of CBD curiosity and usage in exercising populations has exposed an immense gap in the scientific literature concerning the potentially harmful or beneficial effects of various cannabis constituents on exercising individuals' vascular health. As evidence of potential positive and negative influence grows, the safety profile of CBD continues to be provoked [18-19,28].

To determine both acute and chronic effects of CBD on vascular health, further evidence is warranted on cardiovascular profile data and cannabinoid use in exercising populations. Flow-mediated dilation (FMD) ultrasound assessment is technique in cardiovascular research available to evaluate the function of conduit arteries [13]. It involves measuring changes in arterial diameter in response to increased blood flow induced by temporary occlusion and release of blood flow. This assessment has been considered the gold-standard for non-invasive endothelial function assessment

[13,48]. To measure vascular health, FMD ultrasound assessment can provide sports staff and athletes insight into CBD's influence on endothelial function (EF). Utilizing FMD ultrasound assessment to record EF vascular response with the timing of CBD use may enhance awareness of potential changes in EF, therapeutic benefits, and adverse effects that are less apparent than previously evidenced health impairments of general cannabis usage [40].

Examining associations among CBD use, EF, and exercise may increase understanding of how CBD may influence multidimensional constructs of vascular health in exercising populations. Therefore, the primary aim of this review was to critically evaluate emerging evidence of the influence of CBD on endothelial function via FMD ultrasound assessment. The second aim was to consider the influence of CBD, in conjunction with exercise, aerobic training (AT) and resistance training (RT), and its potential effects on vascular health.

1.1 Cannabis

Cannabis, also referred to as *Cannabis Sativa L*, has been used in traditional medicine dating back 12,000 years ago [11,27]. Various cultures have used cannabis to treat and manage clinical ailments and health concerns, such as pain, arthritis, gout, acute and chronic inflammation, anxiety, and depression [11,33]. A well-known component of cannabis, tetrahydrocannabinol (THC), is the primary psychoactive cannabinoid in the plant [32]. THC is principally responsible for pharmacological actions, including psychotropic effects [32]. With recent perspective shifts and legal alternations in the United States [56], cannabis has quickly emerged as a potential therapeutic alternative for exercising populations [5,15,24,27,34,37,43].

1.2 Cannabidiol (CBD)

Although CBD has received positive and negative representations of its potential effects, growing bodies of research are continuing to uncover the non-psychotropic and potentially therapeutic effects of this cannabis constituent. CBD is the second most prominent compound of the cannabis plant, one among 110 known cannabinoids to be extracted [33,54]. Unlike its well-known cannabinoid relative, THC, CBD is the non-psychoactive compound of cannabis and will not elicit a high in users [19,54]. Previous studies [18-19,25] have described CBD as being non-intoxicating and non-addictive, with an excellent safety profile. Prior clinical studies have demonstrated that high doses of oral CBD do not cause psychoactive effects [57-59]. Additionally, CBD has demonstrated anti-inflammatory effects on muscle soreness [9,12,18], cardiovascular hemodynamics [46-47], and improved sleep quality [5,28] in exercising populations. CBD use in epileptic and psychiatric populations have reported CBD-induced drug interactions, fatigue, vomiting, and diarrhea [60,61]. Furthermore, the necessity of CBD exploration in human participants, particularly in active exercising populations, is warranted, given the general safety profile and effects of use previously reported.

1.3 Flow-Mediated Dilation (FMD)

The clinical analysis of brachial artery FMD is a prevalent and noteworthy measurement in cardiovascular research, as it is suitable for its superficial nature, low cost, and simplicity of use [13]. It is considered the gold standard for non-invasive assessment of conduit artery EF due to its validation, clinical trial experience, and associated cardiovascular episodes [13]. FMD assessment can be useful for assessing physiological function and mechanistic understandings that may change endothelial and vascular function and structure [48]. To better understand arterial mechanisms and the potential effects of CBD use on vascular health, specific ultrasound techniques and protocols must be determined to investigate the variables of vascular interest best. Brachial artery FMD can be defined as the vasodilatation of an artery, followed by a rise in shear stress and an increase in blood flow [48]. First studied in 1992 by Celermajer and colleagues [6], endothelial function and dysfunction were first assessed via the assessment of the brachial and femoral arteries using a high-resolution ultrasound device, providing a landmark understanding of the early stages of atherosclerosis development.

The diagnostic potential of FMD can provide a direct evaluation of the arterial form and activity. The arterial dilation that transpires post-blood flow occlusion has been documented as a strong precursor of cardiovascular episodes in healthy populations and those with cardiovascular conditions or diseases [21,48]. Given the endothelium's primary role in preserving vascular quality and sensitivity, there is a large importance in maintaining an unimpaired and functional vascular endothelium [38,42]. Therefore, non-invasive methods for evaluating EF, including FMD, may support invaluable indicators for predicting cardiovascular risk factors and alterations in functional status in relation to arterial structure and function [10].

2 FMD and Exercise

Exercise is a viable holistic alternative for improving cardiovascular responsibility, as evidenced by repetitive bouts of improved shear stress [42]. In essential hypertensive patients, impaired brachial artery FMD improvements have been observed in chronic, effective blood pressure reduction interventions [30,46]. However, the mechanisms for improved endothelium-dependent dilator function post-exercise training are lacking [49]. Furthermore, nitric-oxide dependence has been under speculation as such a mechanism but has continued to encourage further investigation.

Regular physical activity has long been regarded as necessary for maintaining and achieving optimal health. The increasing need for preventive strategies to counteract cardiovascular diseases and conditions is of immense epidemiological importance [14,42]. Aerobic training (AT) may be a viable interventional tool with well-documented efficacy for improving EF [2,29,36,42] and reducing the risk of cardiovascular events [13]. In addition, resistance training (RT) has elicited reductions in blood pressure [50] and displayed improvements in overall brachial artery diameter and post-occlusion blood flow [35,38,49]. Although there is an increasing wealth of information about the role of physical activity on the cardiovascular system, details as to what specific dose, frequency, and intensity of AT and RT prescriptions are optimal remains unclear with CBD use. As evidence suggests that AT and RT may be useful independently and in combination on EF via flow-mediated dilation, studies investigating CBD use with AT and RT on EF remain unexplored.

Exercise may directly impact vascular function, arbitrating shear-stress-induced improvements in FMD [2]. While studies have employed pharmacological agonists yielding mixed results, flow-mediated dilation has consistently been enhanced by exercise training programs in various models [2,29,42]. Based on repetitive sessions of increased shear stress, AT has demonstrated, as independent intervention, to benefit cardiovascular function [42]. Exercise training, in general, has also been suggested to lessen serious and minor cardiovascular episodes [2,3,48].

2.1 Aerobic and Resistance Training and FMD

There is a lack of studies supporting a combination of AT and RT exercise in individuals with endothelial dysfunction or aims to improve EF. The lack of scientific literature is of concern due to the well-documented benefits of physical activity in reducing cardiovascular disease [14]. Despite the rapidly increasing body of knowledge surrounding the role of exercise on the cardiovascular system, unidentifiable apertures and details still exist regarding improved EF exercise prescriptions with AT and RT combined. Furthermore, the literature surrounding AT and RT needs to be highlighted and emphasized, as the therapeutic effects are pertinent and noteworthy.

Clarkson et al. [8] investigated whether exercise training could promote endothelium-dependent dilatation in healthy young males. Twenty-five subjects performed a supervised and standardized AT and RT program over 10 weeks. Subject fitness levels markedly improved after the exercise program, reflecting aerobic fitness increases [8]. In addition, FMD improved significantly after the training program [8]. This landmark study suggested that endothelium-dependent reactions in the brachial arteries of healthy young males can be enhanced with AT and RT in a relatively short duration [8].

As endurance exercise has continued to be well-documented as being effective in improving EF and reducing blood pressure, 50 RT studies have also shown increases in average brachial artery diameter and blood flow post-occlusion, respectively [38,42,49]. However, there is a pronounced lack of studies supporting AT and RT utilized in combination in patients with endothelial dysfunction via FMD assessment [17].

3 FMD and CBD

A limited number of studies have investigated the hemodynamic impact of CBD use in human populations [7,22,42,46-47]. Even fewer studies have explored using CBD and cardiovascular function in exercising populations [42,47]. The effects of exercise, at various exercise intensities, have been shown to have an improved or positive effect on FMD assessment values, including resting artery diameter [42], low flow-mediated constriction [42], and arterial stiffness [53]. However, studies investigating 1) the influence of CBD use on FMD in exercising populations and 2) CBD use on FMD with timing of exercise (pre-, during, post-exercise) are lacking.

A pre-clinical trial on the effects of CBD on cardiovascular physiology demonstrated that CBD may elicit endothelial and nitric-oxide-dependent vasorelaxation of isolated arteries [44]. Animal studies have demonstrated that CBD may alter cardiovascular function [4] and myocardial infarct size in ischemia injury [16] to some extent [41,46]. The effect of CBD on cardiovascular markers of vascular health in human trials remains in its infancy.

One study has investigated the influence of CBD on FMD in healthy populations [47]. Sultan and colleagues demonstrated that one single 600 mg dose of CBD had no influence on heart rate or blood pressure in normal conditions in human participants but did display a reduction in stress-induced increases in heart rate and blood pressure [47]. Additionally, repeated CBD dosing (7 days) was shown to increase FMD, enhancing overall EF [47]. Nonetheless, these effects should warrant caution, given the use of FMD to assess the vasodilatory potential of CBD usage warrants future research in addition to this study having a small sample size and CBD effects on EF were only compared to values after the CBD dose, not the placebo [47]. These findings suggest that CBD may potentially aid cardiovascular health in healthy men.

4 CBD and Exercise

Research investigating the use and effects of cannabis with exercise began just over 40 years ago. However, investigations about CBD specifically concerning exercise are less demonstrated. Although researchers began exploring the effect of cannabis on exercise performance early on [23,39,45], studies included various administration methods and doses with no control or placebo groups, and minimal detail about the cannabis being used.

Even though studies have displayed the soothing and anti-inflammatory properties of CBD for numerous conditions [1,31], research regarding CBD use with exercise is sparse [15,18,28]. Exercise-induced muscle damage (EIMD) may ensue in physical soreness, which is often referred to as delayed onset muscle soreness (DOMS) [18]. This condition is often experienced by individuals who exercise beyond their normal training limits [18]. Although DOMS is somewhat assumed to be a minor type of injury, it is one of the most well-documented justifications for inhibited sports performance in athletic populations [18]. Thus, methods and avenues of recovery have become increasingly important in recent sports research, as this could determine physical, mental, and cognitive decrements.

Clinically, various modalities have been examined for physical treatment that may reduce the effects of EIMD DOMS [18]. With the World Anti-Doping Agency's (WADA) [51] recent removal of CBD from the banned substance list, the frequency of CBD use has rapidly risen [40]. CBD use has been suggested to improve and enhance recovery [18,37,40,43]. However, CBD's role and influence on EIMD DOMS and recovery have not been thoroughly investigated. Furthermore, only three studies to date [9,12,18] have explored the effects of CBD use on muscle soreness and recovery from exercise. In order to better understand the effects of CBD use with exercise, it is imperative that researchers further investigate the effects of CBD at the arterial level first in exercising populations.

Cannabis use in combination with physical activity or exercise surveys [24,34,37,43] have recently determined that respondents used cannabis with exercise for a variety of reasons. Lisano and colleagues [24] reported that 77% of respondents claim that cannabis positively affected performance by improving their focus, relaxation, energy, and recovery after a workout. While YorkWilliams et al [55] reported that 77% of survey respondents agreed or strongly agreed that cannabis enhances recovery from exercise, while Pinzone et al [37] reported that 93% of respondents believed that using cannabidiol (CBD) improved their recovery. Although the number of exercising individuals using cannabis or CBD for claims of improving performance continues to grow, there is still a limited scope of evidence-based research examining how the use of cannabis affects exercise physiologically.

3 Conclusion

The rapid increase in CBD use in exercising populations has exposed an immense gap in the scientific literature concerning the potentially harmful or beneficial effects of cannabis constituents on vascular health. As evidence of potential influence on vascular health grows, the safety profile of CBD continues to be in question. To determine both acute and chronic effects, further evidence is warranted on cardiovascular profile data and the impact of CBD on exercising populations. In addition to increasing understanding of the different effects that CBD may have on vascular health and exercise, future studies examining CBD, FMD, and exercise is required.

Using FMD to assess endothelial function with various timings of CBD use with exercise will increase awareness of potential changes, therapeutic benefits, and adverse effects of cannabinoid usage that are less apparent than previously evidenced health impairments of cannabis use. In particular, determining CBD's effects to improve on FMD in exercising populations is an important area for examination, considering that aerobic exercise has been demonstrated to improve endothelial function and FMD. Furthermore, examining associations among CBD use, endothelial function, and aerobic and resistance training may enhance understanding of how CBD may influence multidimensional constructs of vascular health. Illuminating the effects of CBD on FMD and exercise is necessary for both researchers and sports practitioners, given the increasing use of CBD and its potential to interact with cardiovascular function and performance.

Abbreviations

CBD: Cannabidiol
THC: Tetrahydrocannabinol
FMD: Flow-mediated dilation
EF: Endothelial function
AT: Aerobic training
RT: Resistance training
EIMD: Exercise-induced muscle damage
DOMS: delayed onset muscle soreness
WHO: World Health Organization
WADA: World Anti-Doping Agency

Declarations

Ethics Approval and Consent to Participate
No ethics approval was necessary as there were no participants in this review.

Consent for Publication
Not applicable.

Data Availability
Not applicable.

Conflicts of Interest
The authors declare that they have no competing interests.

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Authors Contributions

Kirsten Thornhill: Conceptualization. **Kirsten Thornhill:** Writing – Original draft preparation.

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