CHRONIC CURCUMIN SUPPLEMENTATION: EFFECTS ON ENDOTHELIAL FUNCTION FOLLOWING EXERCISE-INDUCED MUSCLE DAMAGE

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CHRONIC CURCUMIN SUPPLEMENTATION: EFFECTS ON ENDOTHELIAL FUNCTION FOLLOWING EXERCISE-INDUCED MUSCLE DAMAGE

A Thesis for the Degree

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Chapter I

INTRODUCTION

Background

Inflammation is a physiological response to fight off infection and repair injury to the body, whether that be due to trauma or from damaged tissues.[1] Acute inflammation helps to promote recovery and tends to be localized to the region of injury. In conditions such as metabolic syndrome, however, there is an excessive systemic inflammatory response due to the cellular stress that can lead to further damage of organs, and is termed chronic inflammation. Chronic inflammation is linked to a number of different diseases such as cardiovascular disease (CVD) and type 2 diabetes mellitus (TTDM), and is associated with the elevation of circulating inflammatory markers such as C-reactive protein, IL-6, TNF-α, to name a few.[1,2] Due to the constant state of inflammation in the circulation that is present with these diseases, endothelial dysfunction can also occur. Endothelial dysfunction is defined as an inadequate/abnormal vasoreactivity in response to regulatory stimuli.[3-6]

The endothelium has a number of different biological functions within the vasculature; it acts as a barrier between the blood and the tissues, promotes angiogenesis, decreases inflammation and maintains vascular tone.[6] If the endothelium is functioning properly, shear stress initiates nitric oxide (NO) release from the endothelial cells. NO is transformed from the amino acid L-arginine by endothelial nitric oxide synthase (eNOS), thus increasing its bioavailability.[5,7] NO causes the smooth muscle in vessel walls to relax, thus causing vasodilation and, in turn, a decrease in vascular resistance, a reduction in shear stress, and a decrease in inflammation.[5,8-10] When endothelial dysfunction is present, the endothelium does not react normally to the stimuli; thus, NO bioavailability is reduced and vasodilation does not occur.[4,5] Relative to CVD, the reduced vasodilation, particularly when paired with existing plaque formation in the coronary circulation, represents a substantial elevation in the risk of myocardial ischemia and/or infarction.

Anti-inflammatory Interventions

Exercise

Exercise training has been proven to increase endothelial function through the repeated upregulation of eNOS. The mechanism behind the upregulation of eNOS is thought to be the increased shear stress that repeated exercise bouts offer due to the increase in cardiac output and redistribution of blood flow to the working muscle.[11,12] Over repeated bouts, an adaptation to the endothelium occurs resulting in an increase in NO due to the increase in eNOS levels.[5] Arterial diameter also appears to be greater in trained individuals compared to untrained individuals.[6,12,13] On the other hand, it has also been reported that those with identified endothelial dysfunction can benefit the most from the therapeutic effects of a single bout of exercise.[14]

In addition to the effects of chronic exercise, single bouts of exercise have also been shown to have a beneficial effect on endothelial function.[4,13,15] In healthy individuals with proper endothelial function, elevations in NO serve to increase blood flow, thus allowing the transport of large amounts of blood to the working muscle.[4] The beneficial effects of acute exercise on NO bioavailability have been shown to last for at least 24 hours post-exercise. Rognmo et al.[13] reported that NO remained elevated for up to 48 hours after exercise in trained individuals compared to less than 24 hours in untrained individuals.[13]

Supplementation

Several investigators have reported that supplements can decrease inflammatory markers that are found in the body due to injury or chronic disease. Vitamin D has been shown to decrease inflammation in congestive heart failure patients,[16] and marathon runners had decreased inflammatory markers while using vitamin C supplements.[17]

Turmeric is a spice that is used largely in Indian, Middle Eastern, and Southeast Asian cuisine. It gives a number of foods, such as curry and mustard, their yellowish coloring.[18,19] Curcumin is an active ingredient found in the turmeric plant, and is known to have antioxidant and anti-inflammatory properties[18,20], as well as beneficial effects on skeletal muscle.[21] Several researchers have examined curcumin to determine if its antioxidant and anti-inflammatory effects can enhance endothelial function.[15,20] Antioxidants are reducing agents that prevent oxidation of reactive oxygen species (ROS) from occurring, and in turn decrease oxidative stress. ROS is produced naturally in the body, but excessive ROS production can lead to oxidative damage to the endothelium or apoptosis.[21-23] It has been found that curcumin supplementation downregulates TNF-α and IL-6 expressions and secretions, which leads to a decrease in inflammation and oxidative stress.[24] Farhangkhoee and colleagues[22] found that curcumin prevented upregulation of eNOS mRNA production in diabetic rats, therefore bringing endothelial function back to normal. It is known that by decreasing inflammation there can be an increase in the bioavilabliity of NO; however, the mechanism by which curcumin alters endothelial function remains unclear.[15] It should also be noted that most, if not all, of the studies showing beneficial effects of curcumin supplementation used a diseased population.

The poor solubility and rapid metabolism of curcumin limit its health benefits; this has lead researchers to develop a more bioactive form of curcumin to be more readily used by the body.[18,19,22] By attaching curcumin to a hydrophillic carrier, there is increased curcumin concentration in the blood[18], and when comparing Turmeric supplements, which contain about 3% curcumin, to curcumin supplements, curcumin supplements exhibit more antioxidant and anti-inflammatory properties[18,25].

Exercise-Induced Muscle Damage

Strenuous exercise damages muscle tissue, especially if it is unaccustomed exercise with a pronounced eccentric contractile component; this is referred to as exercise-induced muscle damage (EIMD). Research has shown that downhill running is an eccentric exercise that induces EIMD due to the fact that the muscle is undergoing an exaggerated forced lengthening contraction that accentuated the mechanical overload, thus causing muscle damage at a microtrauma level[21,26-28]. EIMD symptoms include: delayed onset muscle soreness[28,29], loss of strength[27,28], swelling[27], increased creatine kinase concentrations due to cell membrane distruption[19,27], impaired vascular function[28], and diminished glucose uptake[30]. These symptoms occur anywhere from 24 hours to 7 days post exercise and are associated with an increase in inflammation and circulating leukocytes[27]. The damaged muscle attracts leukocytes to the area, and then the neutrophils and macrophages release ROS and pro-inflammatory cytokines to repair the damaged tissue.[31] TNF-α is responsible for muscle proteolysis, and is upregulated by IL-6. Other cytokines like NF-κβ are stimulated by ROS.[31,32] The damaged tissue then is repaired and adapts, making it more resistant to subsequent eccentric loads that are placed upon it.[25,27]The acute increase in inflammatory cytokines, leukocytes, and oxidative stress due to ROS after EIMD is similar to those changes observed in a chronic inflammatory state, including the induction of endothelial dysfunction[28].

Supplementation with anti-inflammatories has been investigated in an attempt to reduce the inflammation associated with EIMD. The focus of previous research has been to either identify methods of enhancing performance, or simply to investigate the inflammatory aspects of EIMD. The majority of previous research has been conducted using varying dosages of non-steroidal anti-inflammatory drugs.[16,17,23] Other nutritional interventions have also been investigated.[16,17] There are only a few studies that have been conducted to examine the anti-inflammatory properties of curcumin as they relate to the symptoms of EIMD. Davis and colleagues[20] examined the effect of curcumin supplementation on EIMD in mice that were put through eccentric or concentric exercise. Curcumin supplementation blunted CK release, decreased inflammation and increased post exercise performance.[20] By decreasing inflammation caused by EIMD it is believed that there can be a decrease in all of the EIMD symptoms, most importantly for the purposes of the current investigation, the reversal of endothelial dysfunction that is associated with EIMD.[33] Unlike much of the previous research, therefore, the focus of this project will be to use EIMD as a model to investigate the effectiveness of curcumin as a supplement to reduce inflammation and the symptoms that are associated with chronic inflammatory-related diseases such as CVD and TTDM.

Conclusion

It is known that EIMD, specifically eccentric exercise, elicits inflammation in the damaged muscle. This can lead to symptoms, such as increased CK concentrations[20], poor endothelial function, decreased glucose uptake[30], swelling[26], and hindrance to performance.[34] Research has indicated that curcumin may be able improve all of these responses. By decreasing inflammatory cytokine concentrations, specifically IL-6 and TNF-α, curcumin may be able to reduce the risk of inflammatory diseases like CVD and TTDM. Both of these conditions involve chronic inflammation; however, if curcumin has beneficial effects on acute inflammation, specifically those associated with EIMD, the knowledge gained from this study may be applicable to the chronic inflammatory state.[15,20,29,35,36]

Purpose Statement

The purpose of this study is to examine the effects of curcumin on endothelial function after exercise-induced muscle damage in moderately trained individuals.

Hypotheses

It is hypothesized that:

1. Following EIMD, curcumin supplementation at 250 and 1000 mg/day will lead to enhanced endothelial function when compared to the placebo condition, and the effect will be greater with 1000 compared to 250 mg/day.
2. Following EIMD, curcumin supplementation at 250 and 1000 mg/day will decrease markers of muscle damage such as soreness, circulating creatine kinase levels, decrements in muscle function, and inflammatory cytokines, when compared to the placebo condition, and the effect will be greater with 1000 compared to 250 mg/day.

Significance of the Problem

By developing a curcumin supplementation regimen that can offset the anti-inflammatory responses associated with EIMD, a step will be taken toward understanding how inflammation, in general, can be managed via nutritional intervention. If responses that are associated with chronic inflammation, such as endothelial dysfunction, can be improved with curcumin supplementation, individuals at risk for inflammatory-related diseases can benefit from this non-pharmacological intervention.

Chapter II

LITERATURE REVIEW

Background

The body produces an inflammatory response to fend off infections, heal injuries or broken tissue, and stimulate recovery. These responses are only intended to be mild and short term. Diseases, such as obesity, diabetes mellitus and cardiovascular disease turn the short-term inflammatory response into a chronic condition.[1] A prospective study, conducted by Ridker et. al[2] identified that post menopausal women were more likely to experience a cardiovascular event if they had increased levels of inflammatory markers like CRP-1and IL-6.[2] IL-6 along with ankle- arm index, was found to be a better indicator of coronary heart disease, in 2,191 men and women in between the ages of 70 and 79 years, when compared to CRP-1 and TNF-α.[37] This concluded that cardiovascular disease is associated with endothelial function.

Endothelial Function

Flow mediated dilation (FMD) is a non invasive method used to asses the amount of NO induced vasodilation that the blood vessel is undertaking due to a shear stress. [5,8,38] With the use of ultrasound, changes in conduit artery diameter can be measured. The shear stress of increased blood flow is caused by conclusion of the artery, causing ischemia. When the blood pressure cuff is released the body responds with reactive hyperaemia.[8,38] With proper endothelial function, endothelial cells will use eNOS to synthesize NO and vasodilate the vessels producing an increase in FMD.

There is a known relationship between endothelial dysfunction and age.[4] Lauer et. al[4] compared 29 young participants (25±1 years) and 28 old participants (58±2 years). Ultrasound was used to measure FMD and plasma nitrite and nitrate levels before and after exercise. FMD was poorer in older subjects, compared to young subjects. Baseline plasma nitrite levels tend to decline with age, however this was not significant in this study. Exercise significantly increased plasma nitrite levels in young subjects (107±8 to 143±11 nmol/L), where as the increase was not significant in the older participants (82±10 to 101±14 nmol/L), indicating, that as we age we have a decrease in endothelial function. Inflammation and increased atherosclerosis probably play a key part in this decrease in endothelial function with increased age.[4]

It was found that nitrite levels post exercise are positively correlated to exercise performance, and NOS-dependent. Individuals that exercised at a higher workload produced higher nitrite concentrations post exercise.[9] How long the increases in NO bioactivity remains elevated in the plasma may depend on training status.[13] Individuals that were endurance trained were reported to have increased nitrite levels for up to 48 hours post exercise, when their sedentary counterparts returned to baseline after 24 hours. Trained athletes were also observed to have a larger brachial artery by 10-15% compared to their sedentary counterparts. However they had similar FMD results, indicating that exercise training increased blood carrying capacity to the working muscle.[13]

Anti-Inflammatory Interventions

Exercise

Poor endothelial function can be a pre cursor for the pathogenesis of arthrosclerosis and increase cardiovascular disease risk [4,5,7]. However, it is well known that exercise can increase endothelial function.[4,8,11,12] Allen and colleagues[14] examined the effect of exercise on peripheral artery disease in 28 participants (age 40-75). Subjects free of coronary artery disease were used as baseline controls (n=21). Those in the diseased population were split into either the supervised exercise group (30-40 min of walking 3 times per week for 3 months, under the supervision of an exercise physiologist) or the home exercise group (30 min of walking 3 times per week for 3 months). Using ultrasound they found that brachial artery FMD increased significantly (Δ1.9%) after 3 months of supervised exercise training. Plasma nitrite levels after 3 months of exercise was no longer significantly different from the control group in the supervised group, indicating an increase in endothelial function. This increase in endothelial function was also accompanied by an increase in exercise capacity.[14]

Sun et. al[12] used 2 month old male Sprague-Dawley rats to examine endothelial function based on exposure to high levels of exercise. The four groups consisted of a sedentary group, an acute endurance group (2 hours per day, 5 days a week for 2 weeks), a chronic endurance exercise group (2 hours per day, 5 days a week for 6 weeks), and a chronic intense exercise group (3 hours per day, 5 days a week for 6 weeks). Blood pressure, heart rate and plasma nitrite and nitrate was measured. The rats in the chronic endurance exercise group started trending toward lower blood pressure compared to the acute or sedentary groups, however it was not significant. Interestingly, the chronic intense group had significantly higher blood pressures than the controls. Chronic endurance training significantly decreased heart rate compared to the sedentary. Acute and chronic endurance exercise experienced increases in vasorelaxation due to increased plasma nitrite and nitrate post exercise. However, the chromic intense exercise group had significantly higher plasma nitrite and nitrate levels compared to the other two exercise groups. These results may indicate that there is critical value at which exercise may start to hinder endothelium dysfunction, because it is placing too much stress on the body.[12]

By increasing endothelial function due to exercise the body relearns how to properly react to changes in stress, and therefore, decreasing endothelial dysfunction. Whatever the stress, increased blood flow or increase inflammation, the body knows how to properly activate NO.[6,9]

Supplementations Effects on Inflammation and Endothelial Function

Supplementation is often used to improve the health of individuals with diseases, especially anti-inflammatory supplementation, because so many conditions are linked to inflammation. Vitamin D supplementation (50µg for 9 months) was found to increase anti-inflammatory cytokine IL-10 and decrease proinflammatory cytokine TNF-α, in individuals with congested heart failure.[16]

Several studies have examined curcumin for its antioxidant and anti-inflammatory purposes on endothelial function and oxidative stress.[15,20,24] However, most, if not all of the studies have involved individuals or animals in a diseased population. Farhangkhoee and colleagues examined the effects of curcumin supplementation (150mg/kg) on diabetic induced oxidative stress in Sprague-Dawley rats. Diabetes increases iNOS and eNOS levels, putting the individual in a chronic state of oxidative stress. After four weeks the curcumin supplemented rats saw the greatest reduction in eNOS and iNOS, resulting in a decrease in oxidative stress. The reduction in iNOS and eNOS regulation leads to a reduction in NO savaging.

Ganjali et. al[36] supplemented obese individuals with curcumin (1g/day) for 4 weeks compared to a placebo. Curcumin decreased vascular endothelial growth factor compared to the placebo. High levels of vascular endothelial growth factor can lead to chronic inflammation disorders. There was also a decrease in IL-1β and IL-4. There was no significant difference in the other markers of inflammation (IL-6, IL-8, and IL-10). This may have been due to the small concentration on curcumin given, and its poor bioavailability.[36]

Exercise-Induced Muscle Damage

Downhill Running Responses

Downhill running is a known method to elicit exercise induced muscle damage, because it is a unaccustomed strenuous exercise that requires continuous eccentric contraction. When repeated eccentric contractions take place the muscle is damaged. During this damage intramuscular proteins are lost in the form of creatine kinase and can be found in the blood up to 10 days post exercise.[27] Muscle damage also leads to an acute inflammatory response to repair the damaged tissue. Neutrophils and macrophages invade the skeletal muscle and breakdown the damaged muscle tissues. In doing so they produce ROS and pro-inflammatory cytokines.[1,26,31,39] Liao et. al[32] examined the effects of DHR on inflammatory markers in female rats. Thirty rats were split into five different groups. The rats ran for either 1 or 2 hours on a -10% grade treadmill at 25m/min and were killed at various time points post exercise. By examining the gastrocnemius and vastus lateralis it was found that TNF-α and CK levels continuously increase post exercise for 24 hours compared to the control group. A limitation of the study was that they only examined up to 24 hours post exercise, and some of the effects up of EIMD can last up to several days.[32]

Barnes et. al[28] took 27 (age 18-38) sedentary or recreationally active individuals to examine the effects of EIMD on acute inflammation and vascular function. The participants either completed protocol 1, which used an eccentric bilateral leg press to elicit EIMD, or protocol 2, which used unilateral eccentric elbow flexion contractions. Measurements were taken and blood was drawn 90 min, 24, 48 and 72 hours post exercise. For protocol 1, CRP levels were significantly different from baseline at the 24 and 48 hours. They were also significantly different from the control group at 24 and 48 hours. However, IL-6 concentrations were not significantly different. At 48 hours post exercise pulse wave velocity reached peak, and was significantly different than the control group. This indicates an increase in arterial stiffness. For protocol 2, pulse wave velocity was significantly different from pre at 48 hours. CRP and IL-6 concentrations were not significantly different, but this may have been due to the smaller muscle group used to elicit EIMD. Isometirc strength decreased and soreness increased in both trails.[28] The increase in inflammation causes edema in the tissue.[26] It is believed that the edema and inflammation lead to an increase in soreness and a decrease in strength and performance post exercise.[27] Inflammation after muscle damage is also known to create oxidative stress and decrease endothelial function.[28,39]

Curcumin and Exercise

A few studies have looked at the effect of curcumin and exercise. Both of which are known to increase endothelial function.[4,9,15] Akazawa et. al[15] took 32 postmenopausal women and compared endothelial function of those taking an oral curcumin supplement (25mg) for 8 weeks to those who moderately exercised (aerobic exercise, 2-3days per week) for 8 weeks. Both groups experienced an increase in FMD when compared to their baseline and the control group.[15] These results tell use that curcumin supplementation and exercise both increase endothelial function, and may offset the decline in endothelial function.

Curcumin and its Effects on Exercise Induced Muscle Damage

Curcumin has been shown to have positive effects on exercise induced muscle damage. A study used eccentric exercise (repeated quadriceps squat) to induce muscle soreness after a 30 day supplementation of either BounceBack capsule or placebo. Those in the curcumin supplementation group experienced reduced pain at 6 and 48 hours post exercise compared to their placebo-taking counterparts.[29] The results from this study are a little misleading due to the fact the capsule used also contained vitamin C, which is another known anti-inflammatory[17], making it difficult to decipher which was the beneficial component, curcumin or vitamin C. Drobnic et. al[35] examined the effects of a 200mg/day of curcumin on muscle damage from downhill running. The participants took the supplement 48 hours before the muscle-damaging bout, and continued for 24 hours after. Those in the curcumin group experienced decreased pain post exercise. CK increased in both groups, however the increase was not as significant in the curcumin group. IL-8 was used as a marker of inflammation, and was significantly reduced in the curcumin group compared to the placebo group. There was no difference in oxidative stress between the two groups, however this may have been due to the low concentration of curcumin taken.[35]

Several studies took it one step further and examined the effect curcumin has on exercise induced muscle damage and oxidative stress. Davis et. al[20] found that when mice were given a 10 mg curcumin tablet three days in a row prior to a downhill running bout experienced increase post exercise performance compared to the placebo group. The curcumin mice had longer running time to fatigue and were also able to maintain baseline voluntary running performance, where as the placebo group were only able to run 75% of baseline. The mice in the curcumin group experienced a significantly lower level of creatine kinase concentrations post downhill running exercise by 100% compared to the placebo group, as well as, a blunted increase in cytokine production (IL-6 and TNF-α).[20] These results indicated that curcumin supplementation prior to an exercise-induced muscle damaging exercise can, not only increase performance post exercise, but also decrease inflammation and muscle damaging markers. Kawanishi et. al[21] also experienced reduced oxidative stress following curcumin supplementation in rats, however they did not experience a different in creatine kinase. This may have been due to the fact that curcumin supplementation was given post exercise as opposed to pre.[21] Takahashi et al.[33] used 10 healthy men (26.8±2.0 years) and found that taking 90 mg of curcumin 2 hours before and immediately after a 60 min run at 65% VO2 decreased derivatives of reactive oxygen metabolites post exercise, where as they increased in the placebo group, resulting in a decrease in oxidative stress.[33] However, the exercise was concentric, and thus does not elicit muscle damage, but does show curcumins capacity to increase endothelial function after an acute bout of exercise.

Chapter III

METHODOLOGY

Subjects

Seventy-five moderately trained men (n=38) and women (n=36) between the 19 and 29 years of age volunteered for the study. Sixty-three men (n=31) and women (n=32) completed the study. Moderately trained was defined as completion of 150 min per week of moderate aerobic activity, or 75 min per week of vigorous aerobic activity for the past three months. Subjects were excluded if they had any preexisting hypertension, diabetes, autoimmune disease, if they had received chronic treatment with anti-inflammatory/analgesic/antioxidant drugs in the previous month, or used of any ergogenic aid 9 weeks prior to recruitment. Females that were pregnant or lactating were also excluded from the study. Health status and activity levels were determined by completion of a medical history form. Subjects were recruited from Texas Christian University and the Dallas/Fort Worth community. Texas Christian University Institutional Review Board approved the study, and all subjects read and signed an approved informed consent form. Baseline demographics are presented in Table 1.

Experimental Design

This study employed a two factor design with a between groups factor (curcumin dosage) and a within groups factor (measurements of time). Subjects were randomized into three groups, with each group receiving eight weeks of varying dosages of curcumin or placebo. The curcumin was supplied as a pre-formulated supplement under the trade name, CurcuWIN®. The low dosage group received 250mg/day of curcumin (C250), the high dosage group received1000mg/day (C1000), and the placebo (P) group received a similar quantity of powder containing no curcumin. After preliminary and baseline testing, all subjects consumed a daily dosage of the supplement for 56 days, after which they returned to the lab for post testing. Dependent measures consisted of blood markers of inflammation and muscle damage, and measures of endothelial function, as determined by flow mediated dilation (FMD). See Figure 1 for a diagram of the design and testing schedule.

Subjects were asked to avoid ingesting foods that contain turmeric (ex. curry or mustard) during the 8 weeks. They were asked to complete a 3-day diet record prior to their first visit, as well as, avoid coffee, alcohol, and NSAIDS 24 hours prior to FMD and throughout the testing days. After completing a macronutrient analysis for a diet record, the participants were asked to keep their diet consistent throughout the testing days, and were asked to avoid a high fat diet (> 25% of total calories as fat), as this could interfere with FMD. Exercise was kept constant throughout the supplementation process. They were asked to restrain from physical activity 48 hours prior to baseline and throughout testing days. Females on oral contraceptives reported to the lab on days 10-12 of their cycle for baseline testing and for post-supplementation testing on day 56. Females not on oral contraceptives reported to the lab on day 4-6 of their cycle for baseline and post-supplementation testing.

Experimental Protocol

Preliminary testing. Participants reported to the lab for familiarization testing. They completed medical, exercise and demographic questionnaires. Participants reported having not taken anti-inflammatory medication for the previous 4 weeks, or consumed nutritional supplements and/or ergogentic aids for the previous 9 weeks, through the use of a recruitment questionnaire. A pregnancy test was administered for females. Vitals signs were taken, consisting of blood pressure, heart rate, and temperature (infrared temporal swipe). Height and weight were used to calculate BMI. They were briefed on how the study would be conducted and given instructions on supplementation, diet and exercise. They were given a list of foods that contain curcumin and were told to refrain from ingesting these foods during the supplementation period.

Experimental testing. On every lab visit subjects reported between the hours 0530 and 1000 after fasting for 10-12 hours.

On the first testing day, baseline flow FMD and maximal aerobic capacity (VO_{2max}) tests were performed. The FMD procedure was conducted in a sound-isolated and temperature-controlled room with subjects in a supine position. An Acuson Aspen Ultrasound System (Mountain View, CA) was used to obtain brachial artery images for the FMD procedures. After resting for 10 min, a baseline measurement of brachial artery diameter was taken using a L10 transducer, placed 8cm proximal to the anticubital space along the medial aspect of the arm. The image provided a longitudinal section of the vessel, and diameter was obtained as described below. A blood pressure cuff was then placed 10 cm distal to the anticubital space on the forearm, and inflated to 50 mmHg above their resting systolic blood pressure. It remained inflated for 5 min. Video monitoring of the longitudinal section of the vessel diameter started 30 sec prior to cuff deflation. The cuff was deflated and video was taken for 3 min post inflation. The software packaged, Brachial Analyzer for Research (Medical Imaging Applications, LLC; Coralville, IA), was used to analyze artery diameter. The software condensed the recorded brachial diameter (mm) for every second of the clip. Maximum brachial artery diameter and baseline artery diameter were used to calculate FMD, and are expressed as a percent change from baseline.

The VO_{2max} test was used to establish fitness level and to ensure that training status did not change over the 8 weeks of supplementation. $\dot{V}O_{2max}$ was assessed by an incremental test to exhaustion on a treadmill with gas exchange continuously measured using a Parvo Medics TrueOne 2400 Metabolic Measurement System (Parvo Medics, Sandy, UT). Briefly, this protocol consisted of incremental stages. To start subjects were asked there 5 k time to determine max speed. For the first 4 stages subjects were running at 0% grade. Every 3 min the speed was increased by .5mph. After the first four stages the incline was increased by 2%, and they became 2 min stages. Test was terminated if subjects voluntarily terminated it, were unable to maintain proper cadence, attained age-predicted heart rate, VO2 leveled off with increasing workload, and if RER was 1.1 or greater**.**

Immediately after baseline testing, subjects took a supplement each day for 8 weeks. The supplement was in pill form, and 3 pills were ingested after breakfast each morning. They maintained their normal physical activity level as determined by their preliminary activity questionnaire. Each week during supplementation, the participants reported to the lab to pick up the next week's pills and to fill out a compliance questionnaire. All subjects were required to meet 80% compliance or they were removed from the study.

After 8 weeks (day 56) of supplementation, the participants again reported to the lab. After vital signs were taken, the FMD procedure was performed, using the procedure previously described. Following the FMD procedure, a VO2 max test was performed to reassess aerobic capacity.

The next day (day 57), participants reported to the lab, and vital signs were again taken. The participants then performed a bout of downhill running (DHR). The DHR was performed on a modified TMX 3030c (Trackmaster, Newton, KS) modified to produce a -15% grade. Prior to the downhill run, subjects warmed-up for 5 minutes at a level grade at a speed equivalent to 65% VO2max. American College of Sports Medicine metabolic calculation for the estimation of energy expenditure during running were used to determine the speed, on a level grade, that would elicit 65% VO2max from the previous day. Gas exchange was continuously measured (Parvo Medics) and speed was adjusted, if necessary, to elicit the target of 65% VO2max. After the 5-minute warm-up, the participants completed a 45-minute downhill run at a grade of -15% at the final speed of the warm up. On day 58, 59, and 60 the subjects reported to the lab the hours 0530 and 1000 after fasting for 10-12 hours. During these sessions, vital signs were also taken; and additional FMD procedures were performed on days 58 and 60.

Blood Processing and Analyses

Blood was taken prior to each FMD procedure. On the downhill run day blood was taken prior to the run, immediately post run, and 1 hour post run. On day 59, blood was also taken for post 48 hour.

Prior to each blood sample, with the exception of immediate post-exercise, subjects were placed in the supine position for 10 minutes before any blood was collected to allow for changes in plasma volume shifts. On the downhill and 48 hours post downhill blood collections a single-use vacutainer needle (BD Vacutainer Eclipse, Franklin Lakes, NJ) was used. At all other blood collections a venous catheter (BD Infusion Therapy Saf-T-Intima, Sandy Utah) was utilized to obtain blood samples both prior to and following the FMD procedure. All samples were collected in 10 mL EDTA vacutainer collection tubes (BD K2E Plus CollectionTubes, Franklin Lakes, NJ). Plasma samples were immediately separated by refrigerated centrifugation at 2950 G for 10 minutes. Aliquots were stored in 2mL micro tubes (VWR International, Radnor, PA) at -80°C for later analysis. Creatine kinase activity was determined using a commercial available colorimetric assay (BioAssay Systems).

Statistical Analysis

A three-factor group by time by gender analysis of variance (ANOVA) with repeated measures on the time factor was used to analyze the data. The first factor, "group", had three levels corresponding to the three dosages of curcumin. The second factor, "time", had multiple levels depending on the number of times a particular variable was sampled. The dependent variables were FMD and CK. Differences detected by the ANOVA were clarified using a *Bonferroni post hoc* test. Statistical significance was set at an alpha level of $p<.05$. All analyses were run using SPSS Version 22 (SPSS Inc, Chicago, IL).

Table1. Subject Characteristics

	Condition	N	M±SD
Females			
Age	1	11	20.82±1.54
	2	10	21.50±2.95
	3	11	21.55±2.70
Males			
Age	1	10	20.80±2.10
	2	10	21.30±1.83
	3	11	21.64±1.86

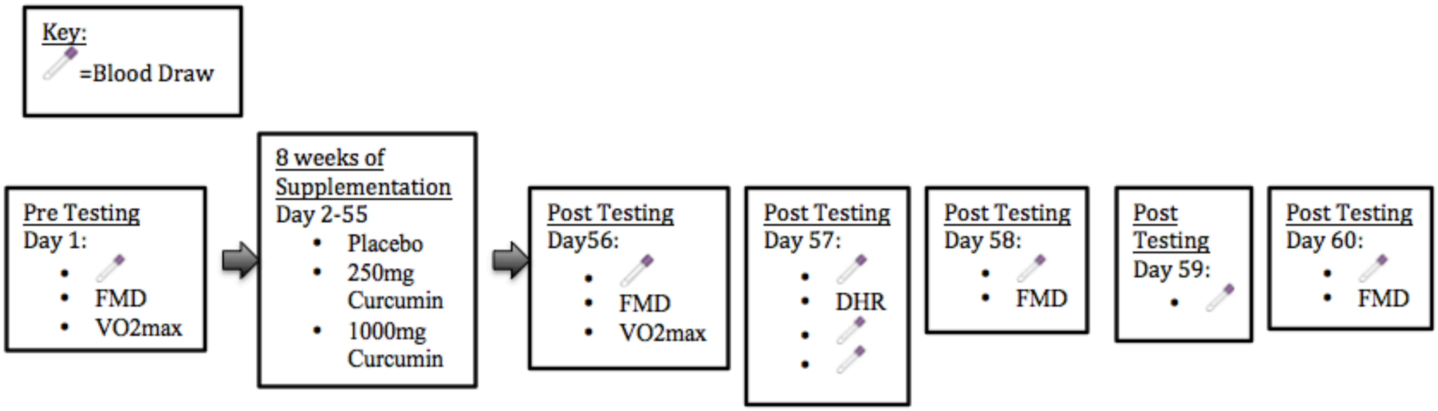

Figure 1. Experimental Testing. =Blood Draw, FMD, Flow mediated dilation; VO2max, maximal aerobic capacity test; DHR, Down hill run.

CHAPTER IV

Results

There were no significant main effects between conditions for age ($p=0.473$), height ($p=.330$), BMI ($p=.938$), weight on day 1 ($p=0.637$), weight on day 56 ($p=.572$), weight on day 57 ($p=.585$), and weight on day 60 ($p=0.620$) (Table 2).

When groups were split by gender, males showed no significant main effects between conditions for age ($p=0.614$), height ($p=0.542$), BMI ($p=0.865$), weight on day1 ($p=0.563$), weight on day 56 ($p=0.627$), weight on day 57 ($p=0.616$), and weight on day 60 ($p=0.611$). Females showed no significant main effects between conditions for age ($p=0.744$), height ($p=0.220$), BMI ($p=0.601$), weight on day1 ($p=0.487$), weight on day 56 ($p=0.258$), weight on day 57 ($p=0.266$), and weight on day 60 ($p=0.093$). There was no significant main effect for time for weight ($p=0.545$), and there was no significant main effect between conditions ($p=0.188$) (Table 2). There were no significant interactions between time by group ($p=0.710$), time by gender ($p=0.525$), group by gender ($p=0.472$), or time by group by gender ($p=0.054$). Females showed no significant main effect for time for weight ($p=0.654$), and no significant main effect between conditions ($p=0.106$). Males showed no significant main effect for time for weight ($p=0.460$), and no significant main effect between conditions ($p=0.543$) (Table 3).

Table 2. Anthropometric Measures and Subject Characteristics

	All		
	P	C250	C1000
n=63	21	20	22
Age (yr)	20.81±1.78	21.40±2.39	21.59±2.26
Height (Cm)	170.58±8.20	173.36±9.23	169.28±9.35
BMI	23.88±2.62	23.83±3.50	23.56±3.14
Weight D1 (kg)	69.79±11.35	72.21±15.16	68.20±14.30
Weight D56 (kg)	70.00±11.19	72.40±14.51	67.97±14.48
Weight D57 (kg)	69.95±11.21	72.24±14.69	67.88±14.51
Weight D60 (kg)	70.21±11.37	72.09±15.03	67.80±15.02

Values are reported as the mean±SD.

Table 3. Anthropometric Measures and Subject Characteristics by Gender

	Females			Males		
	P	C250	C1000	P	C250	C1000
n	11	10	11	10	10	11
Age (yr)	20.82±1.54	21.50±2.95	21.55±2.70	20.80±1.54	21.30±1.83	21.64±1.86
Height (Cm)	165.11±5.38	167.62±5.52	162.64±7.87	176.60±6.36	179.10±8.72	175.91±4.95
BMI	22.79±1.78	21.89±3.21	21.90±1.95	25.07±2.96	25.76±2.70	25.22±3.30
Weight D1 (kg)	62.18±5.99	61.63±10.18	58.16±8.63	78.16±9.89	82.79±11.53	78.23±11.57
Weight D56 (kg)	62.51±6.14	62.36±9.45	57.38±8.40	78.25±9.60	82.43±11.45	78.56±11.10
Weight D57 (kg)	62.51±6.02	62.03±9.38	57.32±8.48	78.13±9.85	82.45±11.66	78.45±11.15
Weight D60 (kg)	62.52±6.29	62.16±9.67	55.64±6.80	78.67±9.58	83.13±11.94	78.85±11.29

Values are reported as the mean±SD.

There was no significant main effect for time for VO_{2max} (p=.073), and no significant main effect between conditions (p=0.380) (Figure 2). When split by gender, males showed a significant main effect for time for VO_{2max} (p=0.015). There was no significant main effect between conditions (p=0.785). Females showed no significant main effect for time for VO_{2max} (p=0.943). There was no significant main effect between conditions (p=0.406) (Figure 3).

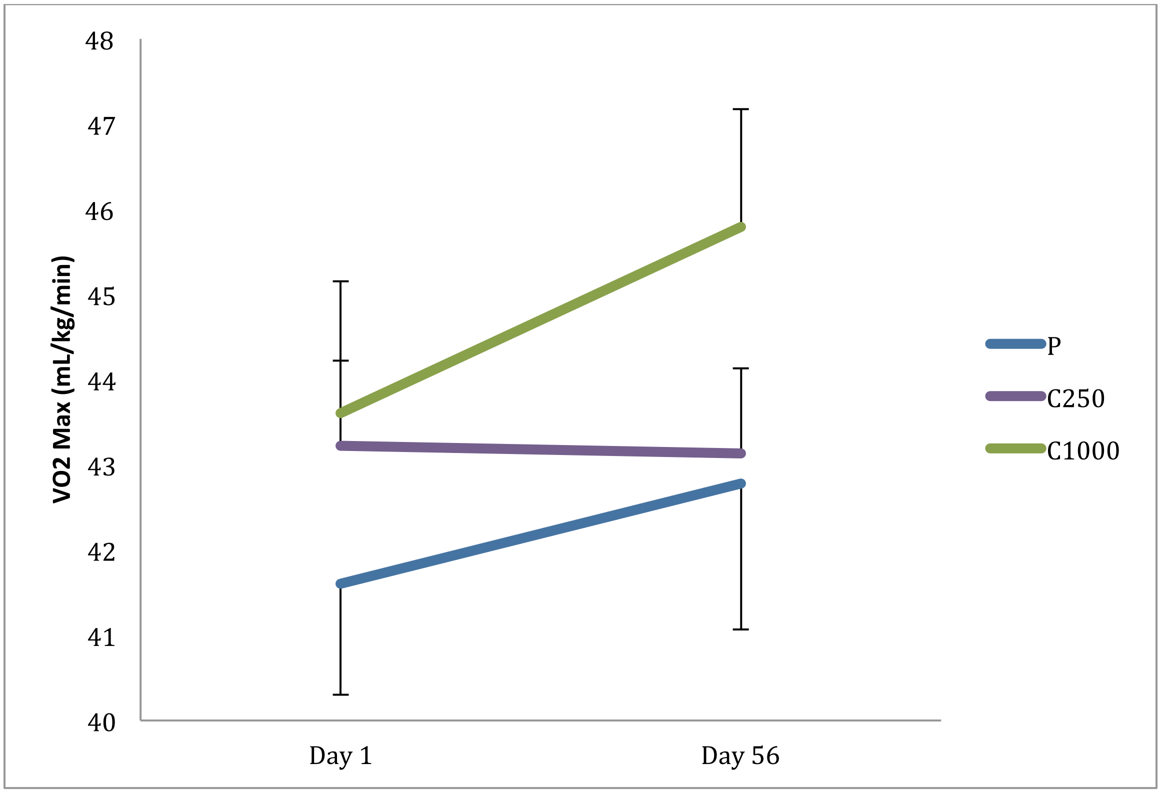

Figure 2. VO_{2max} on day 1 and day 56 by condition. Data reported as mean±SE.

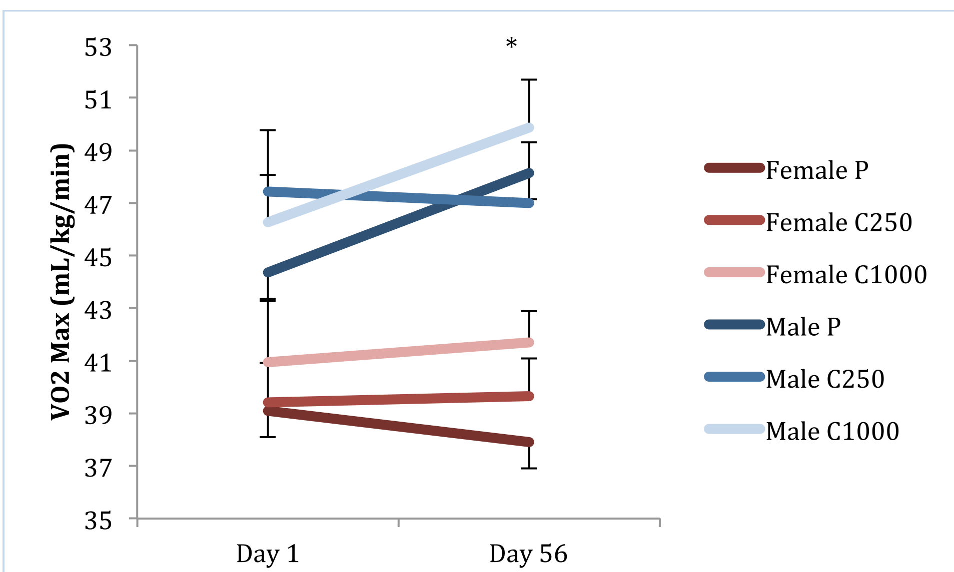

Figure 3. VO_{2max} of males and females on day 1 and day 56 by condition. Data reported as mean±SE. * =Males significantly higher at day 56, $p<0.05$.

Flow Mediated Dilation

There was a significant main effect for time for FMD (p=0.047). Post hoc analyses for time yielded differences between FMD on day 1 and FMD on day 58. There was no significant main effect between conditions (p=0.817) or gender (p=0.678)(Figure 4). There were not significant interactions between time by group (p=0.197), time by gender (p=0.169), group by gender (p=0.801), and time by group by gender (p=0.994). Males showed a significant main effect for time for FMD (p=0.011). Post hoc for time yielded differences between FMD on day 1 and FMD on day 56 and 58. There was no significant main effect between conditions (p=0.632) (Figure 5). There was no significant interaction between time by group (p=0.467). Females showed no significant main effect for time for FMD (p=0.849), and no significant main effect by condition (p=0.993) (Figure 6). There was no significant interaction with time by group (p=0.597).

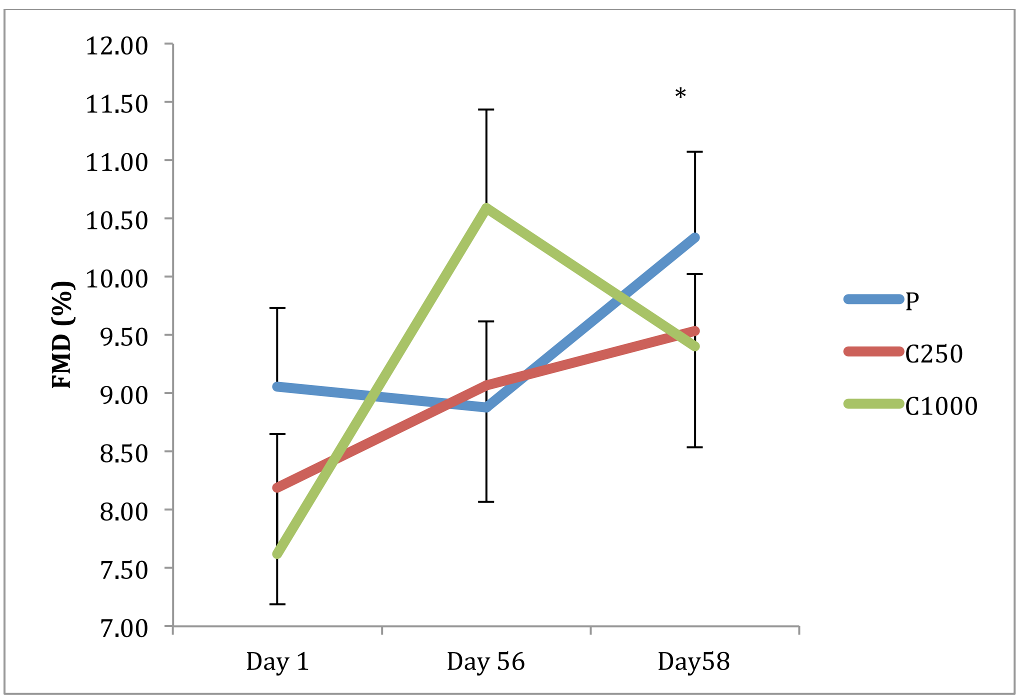

Figure 4. FMD based on condition. Data reported as mean±SE. * = Significantly higher from day 1 p<0.05.

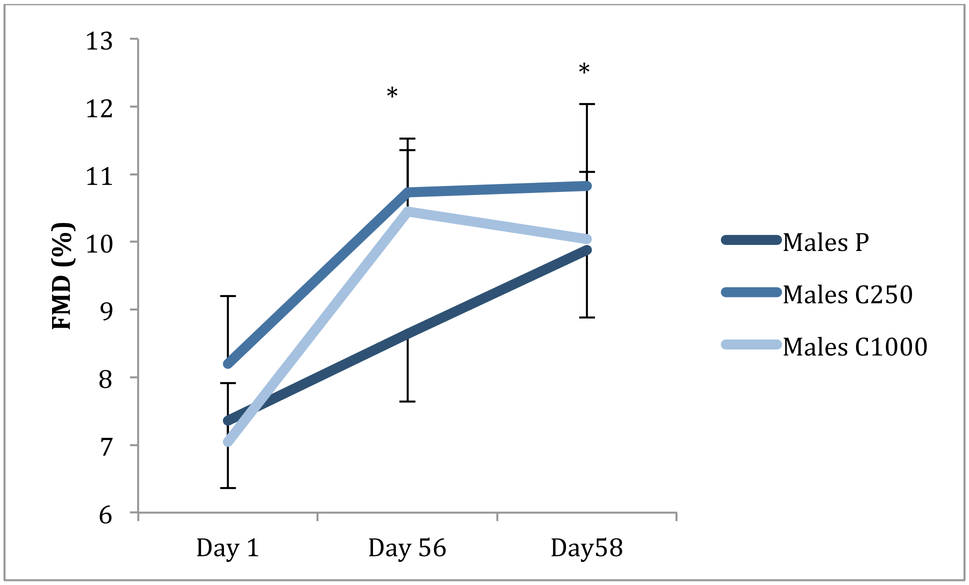

Figure 5. FMD of males based on condition. Data reported as mean±SE, *= Significantly higher from day 1 P<0.05.

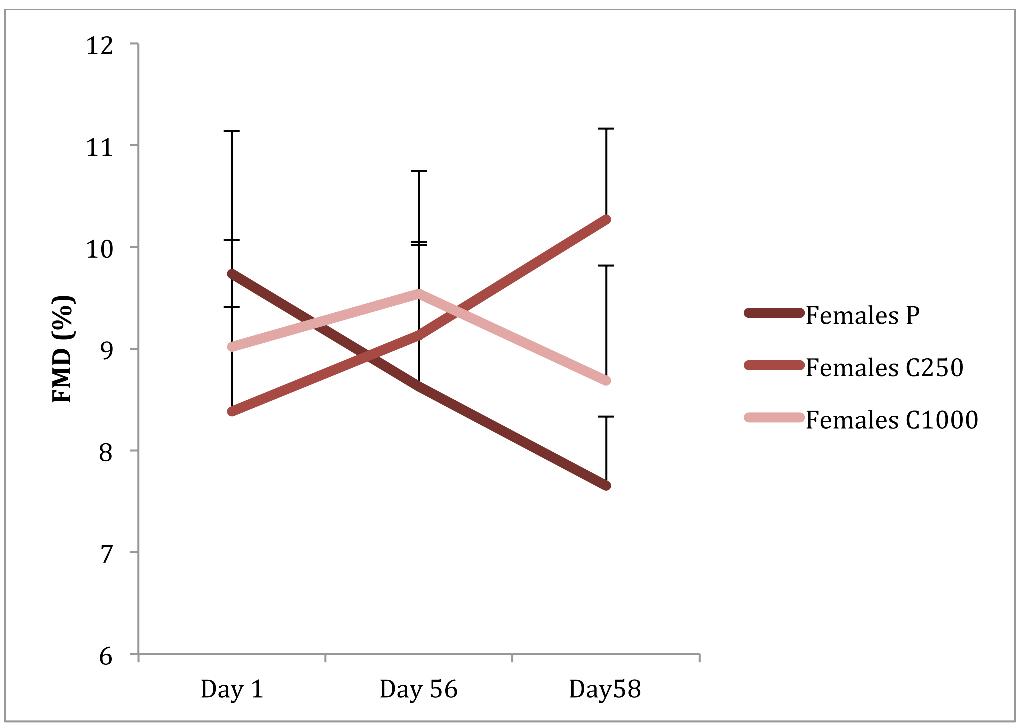

Figure 6. FMD of females based on condition. Data reported as mean±SE.

There was no significant main effect for time for area under the curve (AUC) ($p=0.353$), and no significant main effect between conditions ($p=0.598$) (Figure 7). There was a significant main effect between genders ($p<0.0001$)(Figure 9). There were no significant interactions for time by group ($p=0.617$), time by gender ($p=0.587$), group by gender ($p=0.788$), or time by group by gender ($p=0.429$). For males there was no significant main effect for time for AUC ($p=0.326$), and no significant main effect between conditions ($p=0.932$). There was no significant interaction for time by group ($p=0.550$). Females showed no significant main effect for time for AUC ($p=0.803$), and no significant main effect between conditions ($p=0.355$)(Figure 8). There was no significant interaction for time by group ($p=0.407$).

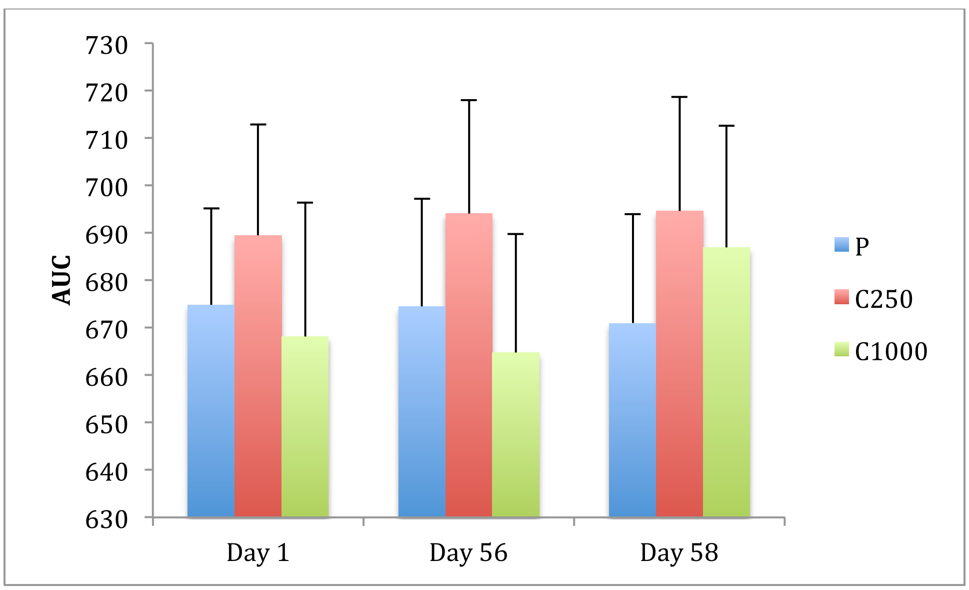

Figure 7. AUC based on condition. Data reported as mean±SE.

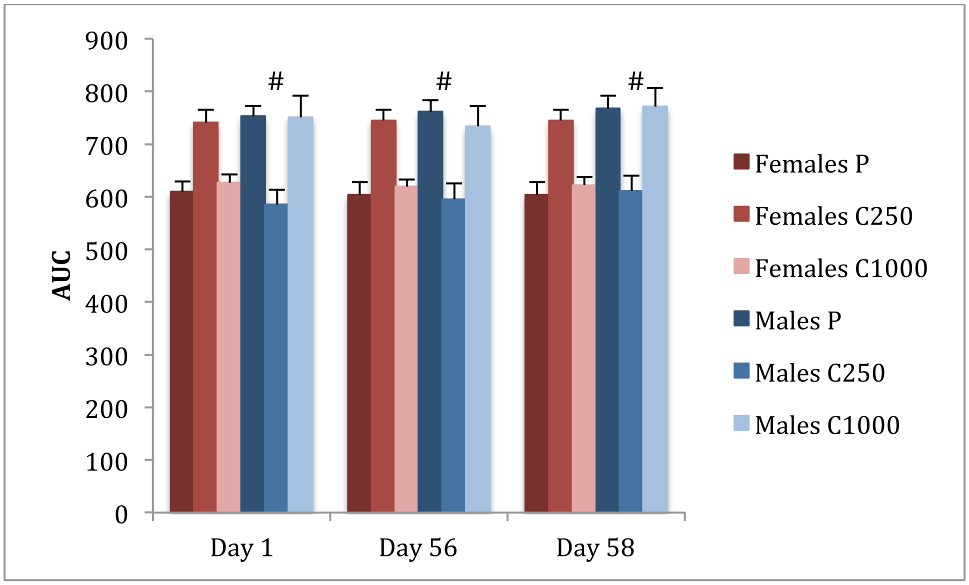

Figure 8. AUC based on gender and condition. Data reported as mean±SE. #= Males significant higher than females, $p<0.05$

There was a significant main effect for time for incremental area under the curve (IAUC) ($p=0.030$). Post hoc analysis for time yielded differences between IAUC on day 1 and IAUC on day 56 and 58. There was no significant main effect between conditions ($p=0.580$). There was a significant main effect between genders ($p=0.031$) (Figure 9). There were no significant interactions for time by group ($p=0.525$), time by gender ($p=0.190$), group by gender ($p=0.870$), or time by group by gender ($p=0.996$). Males showed no significant main effect for time for IAUC ($p=0.058$), and no significant main effect between conditions ($p=0.848$). There was no significant interaction for time by group ($p=0.953$). Females showed no significant main effect for time for IAUC ($p=0.154$), and no significant main effect between conditions ($p=0.567$) (Figure 10). There was no significant interaction for time by group ($p=0.374$).

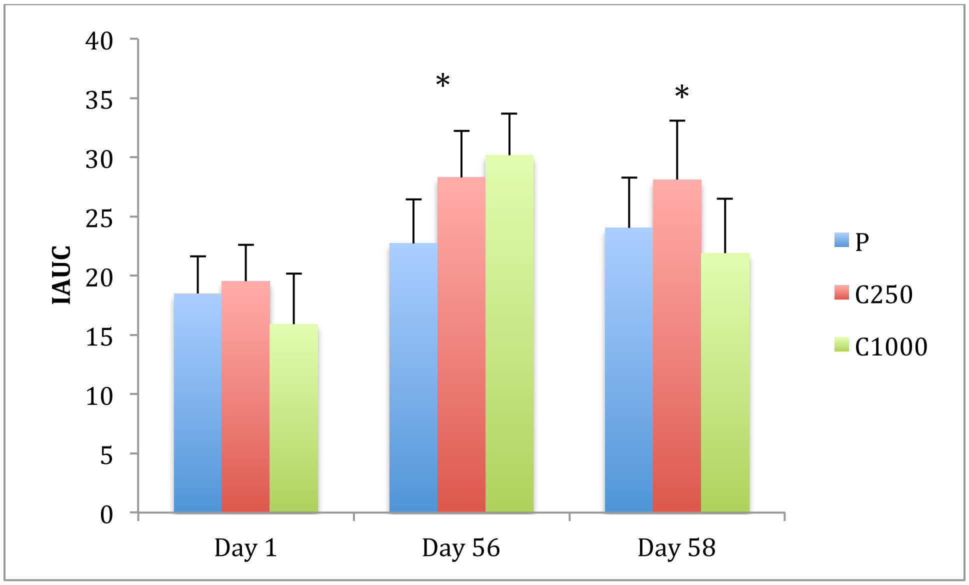

Figure 9. IAUC based on condition. Data reported as mean±SE. *=Day 56 and 58 significantly higher from day 1 $p<0.05$

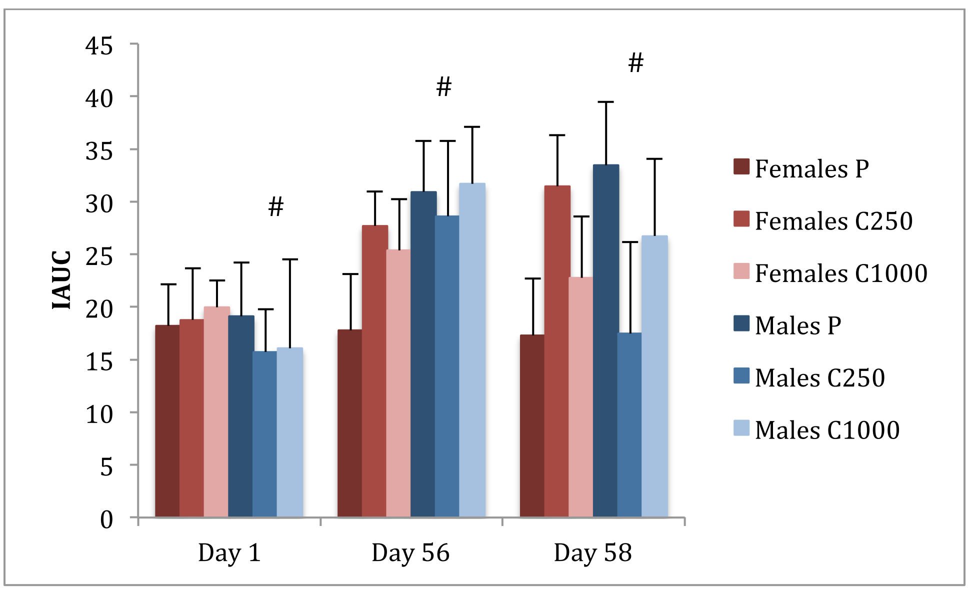

Figure 10. IAUC for genders based on condition. Data reported as mean±SE. # = Males significantly higher than females, $p<0.05$

Creatine Kinase

There was a significant main effect for time for CK ($p<0.0001$). Post hoc analysis for time yielded significant differences between multiple time points as shown in Figure 11. There was no significant main effect between conditions ($p=0.290$). There was a significant main effect between genders ($p=0.001$). There were no significant interactions between time by group ($p=0.306$), time by gender ($p=0.153$), group by gender ($p=0.326$), or time by group by gender ($p=0.738$). Females showed a significant main effect for time for CK ($p=0.001$). Post hoc analysis for time yielded significant differences seen in Figure 12. There was no significant main effect between conditions ($p=0.994$). Females showed no significant interaction for time by group ($p=0.158$). Males showed a significant main effect for time for CK ($p<0.0001$). Post hoc analysis for time yielded significant differences seen in Figure 13. There was not significant main effect between conditions ($p=0.159$). Males showed no significant interaction for time by group ($p=0.702$).

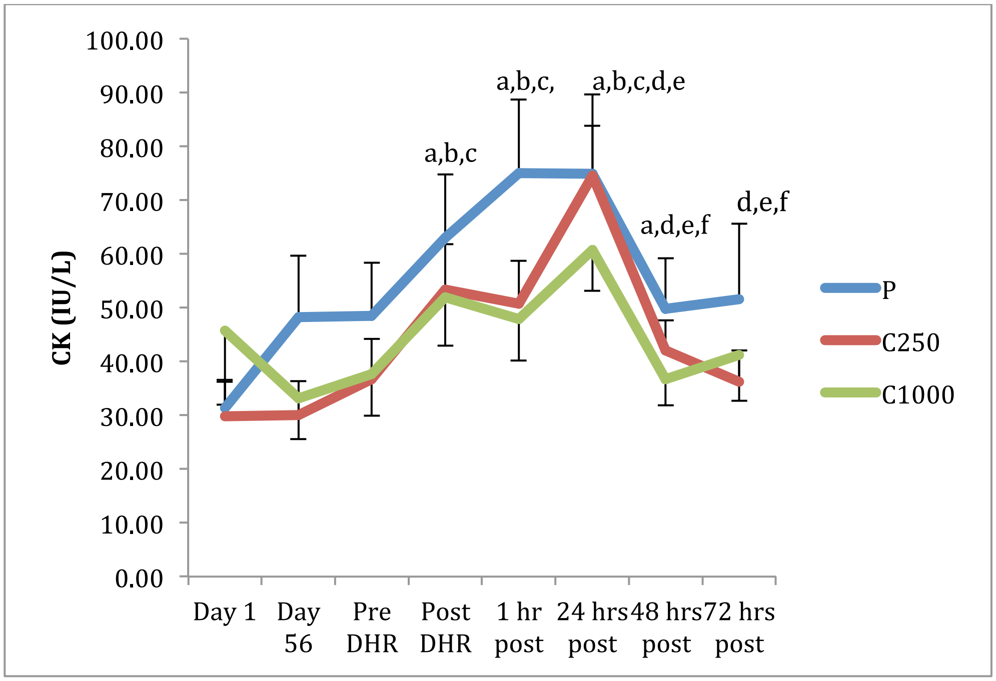

Figure 11. Creatine kinase based on condition. Data reported as mean±SE. a=Significant from day 1 $p<0.05$, b Significant from day 56, c=Significant from Pre DHR, d=significant from Post DHR, e=Significant from 1 hr post, f= significant from 24 hr post

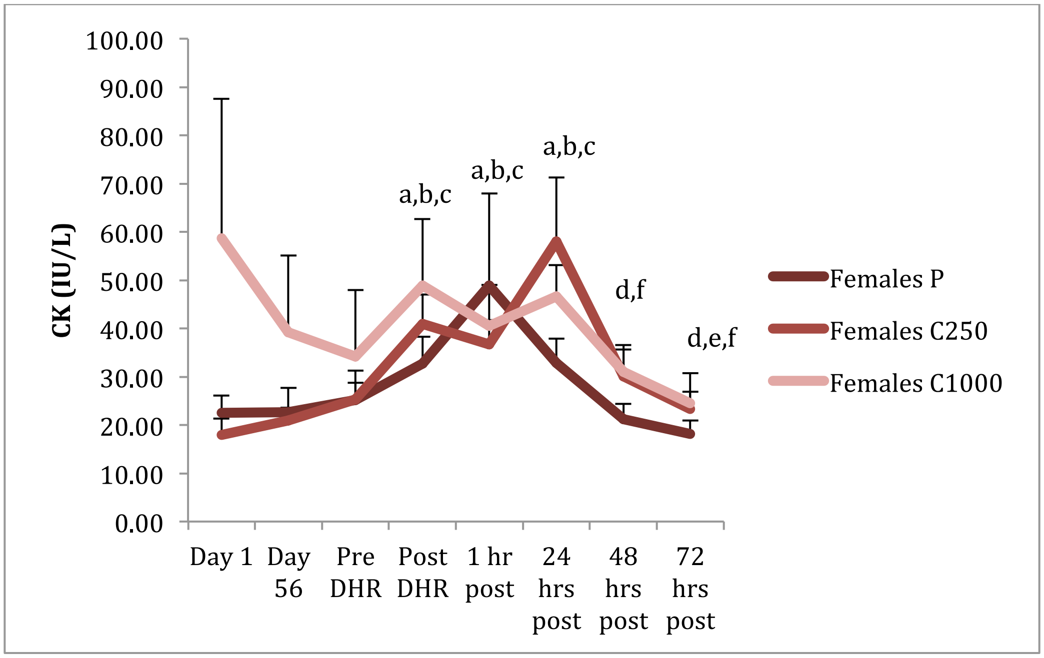

Figure 12. Creatine kinase for females based on condition. Data reported as mean±SE.

a=Significant from day 1 $p<0.05$, b Significant from day 56, c=Significant from Pre DHR, d=significant from Post DHR, e=Significant from 1 hr post, f= significant from 24 hr post

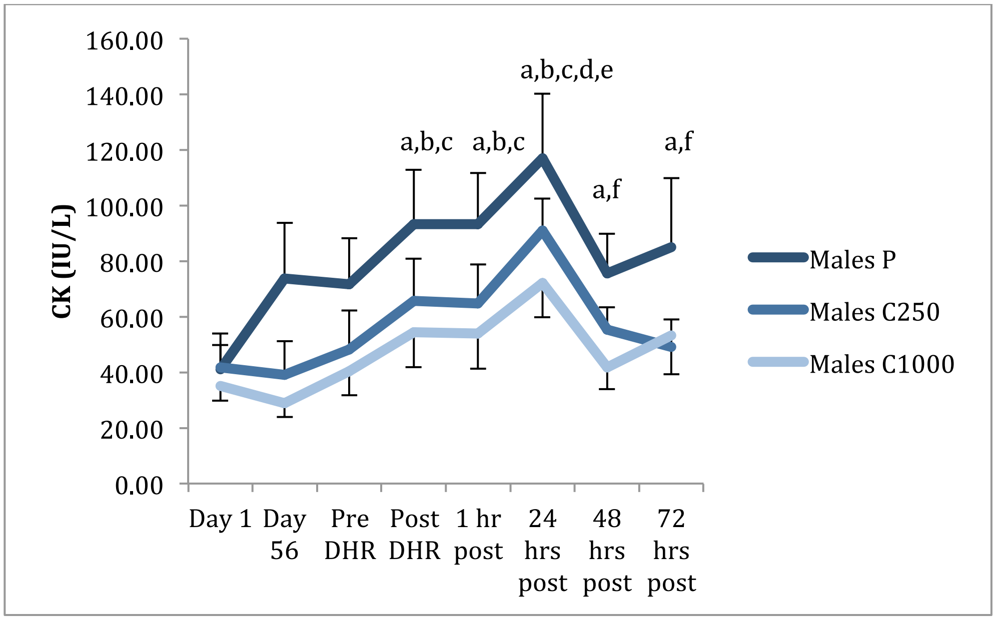

Figure 13. Creatine kinase for males based on condition. Data reported as mean±SE.

a=Significant from day 1 $p<0.05$, b Significant from day 56, c=Significant from Pre DHR, d=significant from Post DHR, e=Significant from 1 hr post, f= significant from 24 hr post

Chapter V

DISCUSSION

The principle finding of the study was that 45 min of downhill running at 65 % VO_{2max} did elicit muscle damage; however, curcumin supplementation did not attenuate muscle damage as indicated by plasma levels of CK. In addition, curcumin supplementation did not alter endothelial function either before or after the muscle damage was induced. To the author's knowledge, this is the first study to examine the relationship between EIMD, endothelial function, and curcumin supplementation in humans.

Muscle Damage

After completion of the DHR, creatine kinase levels were significantly elevated immediately post exercise and remained elevated until 24 hrs post exercise. Our results are in agreement with the findings of Barnes et al.[28] who reported that CK levels peaked at 24 hrs post exercise. They used an eccentric bilateral leg press and unilateral eccentric elbow flexion to elicit muscle damage. Barnes et al.[28] and other investigators[20,27] have shown that CK levels are an indirect marker of muscle damage and the associated inflammation. The eccentric exercise forcibly lengthens the contracting muscles in combination with greater mechanical overload, thus causing microtrauma evidenced by the presence of z-line disruption.[27] Over the course of the subsequent 24-48 hours, an inflammatory response takes place that is responsible for inducing the secondary damage that is associated with cell membrane disruption and the leakage of CK into the circulation.[26,27] According to previous researcher, our CK results put our subjects in the low responders category, which may be due to the fact that DHR normally elicits lower responses than isolated high-force eccentric exercises such as forced lengthening of the elbow flexors.[27] Lower responses could also indicate that individuals could have been “pre adapted”, a phenomenon observed following a single bout of novel, eccentrically biased exercise.[40] Our subjects were recreationally active individuals, but it is unlikely that they had engaged in enough DHR to produce a substantial adaptation. Even when trained runners are subjected to 45-60 min of DHR, they experience a pronounced elevation in CK.[34] Regardless of the reason for the relatively low CK responses, the important issue relative to the design of this investigation was whether the EIMD was severe enough to induce an inflammatory response that could then be the basis for studying the potential anti-inflammatory effects of curcumin. Without biomarkers of inflammation we had to rely on indirect markers of muscle damage, such as muscle soreness. Soreness responses did increase post EIMD, and were used to indicate that inflammation was produced. Soreness responses are reported elsewhere.

In the current investigation, we showed no significant difference in CK response across conditions. This is opposite of what Davis et al.[20] observed when looking at DHR and curcumin supplementation in rats. They reported that curcumin supplementation blunted both inflammation and CK levels after DHR. We hypothesized that chronic supplementation with curcumin would attenuate the effects of EIMD; however, the statistical analysis revealed there was no difference between groups, suggesting that curcumin supplementation did not have an effect on markers of muscle damage. Curcumin is rapidly metabolized in the body and poorly absorbed in the gut causing it to be under-utilized by the cells.[18] In our investigation, the formulation used was designed to maximize the availability of the curcumin in the tissues via the addition of a hydrophilic carrier, the purpose of which was to decrease metabolism and increase absorption. This may have been ineffective despite results from a previous study that stated the curcumin with a hydrophilic carrier had a 45.9 fold increase in absorption. [18] If curcumin concentrations did increase in absorption after ingestion, the results we experienced may have been due to curcumin not exerting a strong enough anti-inflammatory effect to at the cellular level to decrease EIMD. Further research using the measurement of plasma levels and possibly tissue levels of curcumin is needed to better explain the current findings.

Flow Mediated Dilation

Endothelial dysfunction has been associated with many physiologically-based diseases and has many contributing factors such as age, sodium intake, cholesterol levels, glycemia, and comorbidities like obesity and diabetes.[4,6] In addition, an elevated level of systemic inflammation is one of the more common contributors to endothelial dysfunction. Current literature suggests that EIMD induces enough inflammation to produce endothelial dysfunction.[28,41]

Endothelial function remained constant over the eight weeks of curcumin supplementation prior to the introduction of EIMD, regardless of dosage group. Curcumin research thus far has dealt with individuals in a diseased state, and specifically those that already have endothelial dysfunction. [15,24,36,42] Previous research supports the idea that curcumin supplementation can increase endothelial function when an individual has chronic inflammation and resulting endothelial dysfunction. Our population was young, healthy, and disease free individuals, this is the main reason we did not see any significant difference between endothelial function pre and post supplementation. Future research should examine this novel form of curcumin on individuals that have chronic inflammation and known endothelial dysfunction.

Because EIMD has an acute inflammatory component to it, it seems logical to anticipate that FMD following a bout of DHR would be impaired. Despite our original hypothesis that EIMD would induce an acute state of endothelial dysfunction (decrease FMD), there were no significant differences over day 56 and day 58. Burr et al.[41] examined moderately trained men and found that a bout of DHR induced arterial stiffness at 48 hrs post DHR. The fact that they found dysfunction at 48 hrs and not 24 hrs may help explain our results since it may be that if we had examined the FMD response over a longer recovery period, a significant level of endothelial dysfunction may have appeared. While we expected FMD to be negatively affected and reduced following a bout of DHR, it is likely that the lack of significance is due to the age and the healthy status of the individuals. Endothelial function decreases with age, as well as, decreases with declines in health. As an individuals ages there is an increase in systemic inflammation either caused by cardiovascular disease, arthrosclerosis, type 2 diabetes, etc. Al Suwaidi et al.[3] measured those at risk for experiencing a cardiovascular event, and found that those with severe endothelial dysfunction were the only individuals that had a cardiac event. Our individuals were young and free of disease and were better able to adapt to an increase in inflammation.

Researchers state that the vasculature undergoes a structural adaptation when an individual becomes trained. Rognmo et al.[13] found that young (age<25 years) trained and sedentary men had similar FMD responses, except trained individuals had larger artery diameters, both groups were free of any health risks. The larger artery diameters are beneficial in the fact that there needs to be a larger shear stress in order to elicit endothelial dysfunction.[40] Even though the DHR did induce muscle damage, there may not have been enough inflammation to induce endothelial dysfunction.

There was a significant main effect for time between day 1 and day 58, with day 58 being larger than day 1; this is believed to be due to a training adaption to the technique. Because FMD is an autonomic response and subjects becoming more familiar with the environment and less anxious may have played a role in the significance between day 1 and 58. This leads to the conclusion that a familiarization day is needed in future studies, as to introduce the subjects to the procedure and decrease subject anxiety.

Our original hypothesis was that curcumin supplementation would improve EIMD-induced endothelial dysfunction; however, there was no significant difference between groups. The lack of significance may have been due to the fact that there was no endothelial dysfunction to improve due to reasons already stated. FMD, AUC, and IAUC help to eliminate some of the noise seen with individual clips by combining all clips at each time point (using a trapezoidal method), and provides a more global view of the endothelial response. When analyzing FMD using these data we observed that males elicited greater FMD responses than females. The significant difference in AUC between males and females is normally due to males having larger artery diameters, so naturally they would have larger AUC. Normally, IAUC is used to eliminate the anatomical differences between male and females. IAUC still showed a significant main effect for gender, with males having larger IAUC than females. This is most likely due to the lack of familiarization phase and noise in the data due to subject movement.

Conclusion

The results of the study indicated that a single bout of DHR does in fact elicit muscle damage; however, chronic curcumin supplementation did not attenuate CK levels. EIMD did not produce a decrease in FMD as a measure of endothelial function during the recovery period following the damaging exercise. This was similar across groups. The lack of change in the placebo group leads to the conclusion that EIMD based on a DHR did not elicit enough of an inflammatory response to induce endothelial dysfunction in recreationally active individuals. Based on these results, 8 weeks of curcumin supplementation did not improve endothelial function or markers of muscle damage following a bout of DHR.

Strengths

This study used a randomized, double blind, placebo controlled design. The trials were tightly controlled and there was a large subject number in each group, thus giving the study adequate statistical power. Subjects arrived fasted on all 6 days and reported to the lab in the mornings before 1000. Diet records were taken for 3 days prior to the first trial and repeated after 8 weeks of supplementation as to not alter FMD. Exercise, alcohol, and caffeine were controlled prior to and throughout trial days.

The same technician performed all FMD procedures in order to eliminate intertechnician variability. In analyzing FMD, the same technician analyzed all 3 days worth of FMD results for a given subject, again, to keep intertechnician variability to a minimum. FMD was conducted in a temperature-controlled room, in order to eliminate any thermoregulation effects on the body. Gas analysis was used to monitor exercise intensity to make sure DHR running intensity was exactly 65% VO_{2max}.

Limitations

A major limitation of the study is that inflammatory markers were not quantified. It is widely accepted that CK responses are a good indicator of muscle damage; however, inflammation and CK are not always in agreement, thus limiting the accuracy of the conclusion about the relationship between muscle damage and the inflammatory state of the subjects after the DHR.

Nitrite and nitrate concentrations indicate the amount of NO activity that took place due to reactive hyperemia. A disadvantage is that without these concentrations to compare FMD data to, one cannot conclude that NO was the mechanism for vasodilation after cuff inflation. It should also be noted that a familiarization trial to FMD might contribute to more accurate results.

Future Studies

Future studies need to examine the effect of DHR and the associated inflammation on FMD for up to at least 72 hrs post exercise since it may be that more delayed responses would statistically different. Although CK is a well-established marker of muscle damage, markers of inflammation should be taken so that a clear-cut conclusion can be made. Another consideration that can be made is examining the effects of curcumin supplementation on metabolic factors following EIMD. Research has shown that inflammation can alter glucose uptake and insulin sensitivity. Curcuminoid concentration should be measured in the blood and muscle biopsies taken to verify that the curcumin is being metabolized and utilized by the body, and not excreted immediately.

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ABSTRACT

Chronic Curcumin Supplementation: Effects on Endothelial Function Following Exercise-Induced Muscle Damage.

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Introduction: Chronic inflammation is linked to endothelial dysfunction. Supplementation with curcumin, an anti-inflammatory, has been proved to improve endothelial function in individuals with chronic inflammation. Exercise-induced muscle damage induces acute inflammation, and can lead to a decrease in endothelial function. **Purpose:** The purpose of this study was to examine the effects of curcumin on endothelial function after exercise-induced muscle damage in moderately trained individuals. **Methods:** Seventy-five moderately trained men (n=31) and women (n=32) volunteered for the study. Subjects were randomized into one of three groups for supplementation. The low dosage group received 250mg/day of curcumin (C250), the high dosage group received1000mg/day (C1000), and the placebo (P) group received a similar quantity of powder containing no curcumin. Each subject supplemented for two months. Anaerobic capacity, endothelial function, and baseline anthropometric testing were performed prior to 8 weeks of supplementation. Post supplementation subjects reported to the lab five consecutive days. The same baseline tests were retested followed by a 45 min downhill run at 65% VO2max to induce muscle damage. Endothelial function and blood markers were measured post muscle damage. **Results:** There was no significant difference between groups for FMD, AUC, and IAUC. There was significant increase in creatine kinase post down hill run in all groups. **Conclusion:** Curcumin supplementation did not improve endothelial function following exercise induced muscle damage.

Elizabeth Sanders

QUALIFICATIONS

- Advocate for individuals of all backgrounds, who is passionate about providing physical activity, nutritional and health knowledge, to improve quality of life.
- Collaborates well with members of teams to provide optimal care and performance
- Works well in a research setting to maintain proper research protocol

EDUCATION

Texas Christian University May 2015
Fort Worth, Texas
Master of Science in Kinesiology, Emphasis: Exercise Physiology

Texas Christian University May 2012
Fort Worth, Texas
Bachelor of Science in Kinesiology - Major: Movement Science

TEACHING & LABORATORY EXPERIENCE

TCU Harris College of Nursing and Health Sciences August 2013- May 2015
Graduate Assistant

- Develop and execute research projects, including implementing design, data collection, and manuscript composition
- Worked as the primary investigator for clinical trials
- Perform and analyze VO2 Max tests on a treadmill and ergometer
- Write IRB, informed consent, and screen for adverse events in study trials.
- Proficient and valid in the implementation of Flow Mediated Dilation for endothelial function
- Complete labs and experiments in an environmental controlled chamber
- Execute glucose and lactate assays, as well as, heat shock protein ELISAs
- Familiar with the use of a Multiplex ELISA
- Proficient in the use of a spectrometer and hematology analyzer
- Offered nutritional knowledge as part of the Special Olympics-Healthy Athletes program
- Created health awareness for uninformed populations
- Adept in phlebotomy through a single stick or intravenous catheter to obtain blood samples.

TCU Harris College of Nursing and Health Sciences August 2013- May 2015
Teacher Assistant

- Provide assistance in teaching Exercise Physiology, Anatomical Kinesiology, Intro to Kinesiology, Exercise Psychology and Body Conditioning courses
- Design curriculum and syllabus for body conditioning undergraduate course
- Instruct exercise physiology lab and create group exercise programs for the undergraduate students
- Instructed and held bi-weekly review sessions over basic anatomy and physiology of the human body, as well as, exercise physiology
- Performed and graded labs and assignments
- Prepared and taught a course on stress and stress management
- Filled in for professors in the class room when needed

RESEARCH

Masters Program

"Chronic Curcumin Supplementation: Effects on Exercise Induced Muscle Damage and Endothelial Function." 2014-2015

- Masters Thesis
- Investigated different dosage responses of curcumin supplementation on vascular function after a muscle-damaging bout of exercise
- Perform and analyze flow mediated dilation on the brachial artery
- Analyzed blood using a spectrophotometric assay for creatine kinase concentrations
- Perform statistical analysis using SPSS
- Proposed and defend significance of the project and findings
- Supplement 73 participants for 2 months, and induced muscle damage using down hill running
- Create a study protocol to adequately test the hypothesis

"Validity of Nutrition Knowledge Questionnaire for Adults with Learning Disabilities," 2013

- Presented at Texas American College of Sports Medicine meeting, 2013
- Collected anthropometrics and nutritional data at Special Olympics-Healthy Athletes
- Compared Athletes nutritional intake to their parent or caregiver to test validity of questionnaire used by the Healthy Athletes Program

"Effect of Eating Speed at Breakfast on Appetite and Daily Food Consumption." 2013

- Research Assistant
- Collected blood samples from a catheter to determine levels of glucose, insulin, and GLP-1 in the blood prior, during, and immediately following meal consumption.
- Monitored eating speed and study protocol, and assisted in subject recruitment
- Performed an ELISA to identify various gut hormones

Bachelors Program

"Determining the Critical Value: Baseball Bats of Varying Moments of Inertia." 2012
Senior research project

- Used PEAK Motion Analysis System to obtain mechanical data of baseball players swing after warming up with varying bat weights
- Designed and implemented study protocol to test the hypothesis
- Digitized data to obtain angular momentum of bat mechanics and velocity

WORK EXPERIENCE

Texas Christian University August 2013 - May 2015
Fort Worth, Texas
Departmental Assistant

- Graduate assistant and teaching assistant duties

SporTherapy September 2012 - September 2013
Fort Worth, Texas

- Instruct and demonstrate routines to patients, focusing on proper mechanics
- Introduced to aquatic therapy and its benefits for the rehabilitation process
- Communicate effectively and professionally with patients, teammates, and colleagues

- Created a tobacco awareness flyer for patients

VOLUNTEER EXPERIENCE

Special Olympics-Healthy Athletes Program October 2013 - March 2014
College Station and Austin, Texas
- Provided health and nutritional knowledge to athletes

Ironman Sports Medicine Institute July 2014
Houston, Texas

Make Promises Happen March 2012
Guthrie, Oklahoma
- Provides outdoor recreational activities for individuals of all ages with disabilities.

Baylor Institute of Rehabilitation September 2012 – October 2012
Dallas, Texas

Texas Health Care Bone and Joint Clinic June 2012
Fort Worth, Texas

Texas Health Ben Hogan Sports Medicine July 2012
Fort Worth, Texas

PROFESSIONAL MEMBERSHIPS AND CERTIFICATIONS

American College of Sports Medicine, Member, Present
Texas Regional Chapter- American College of Sports Medicine, Member, 2013-Present
- Attended, present poster, and organized meeting, 2013

CPR Certified

AWARDS

Outstanding Academic Achievement Award, April 2015
Dean's List, 1 Semester