

**“PUMPING YOU UP” THE CARDIOVASCULAR EFFECTS OF OVER-THE-
COUNTER WEIGHT LIFTING SUPPLEMENTS**

By

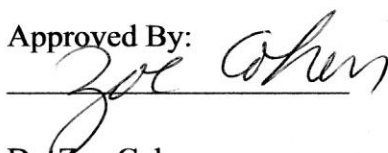
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A Thesis Submitted to The Honors College
In Partial Fulfillment of the Bachelors degree
With Honors in
Physiology

THE UNIVERSITY OF ARIZONA

MAY 2013

Approved By:



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Honors area (eg Molecular and Cellular Biology, English, Studio Art):

PHYSIOLOGY

Date thesis submitted to Honors College:

4/24/2013

Title of Honors thesis:

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Abstract

Subsequent to the analysis of a pre-workout supplement, during-workout supplement, and post-workout supplement, it was concluded that only the post strength training recovery supplement (Optimum Nutrition's™ Gold Standard 100% Whey Protein) was able to successfully fulfill all of the company's claims as well as proved the most beneficial. It was noted that the other two types of supplements had some potentially negative effects on a human's cardiovascular system, were not necessarily beneficial for strength training exercisers, and contained various ingredients with both valid and invalid company claims. This review of the cardiovascular (CV) system in congruence with strength training supplements concludes the vital connections between the two are important and should be heavily considered upon use of supplementation resembling any of the three reviewed.

Table of Contents

Introduction	I
Overview of the Cardiovascular System	II
Heart Anatomy Overview	II
Blood Anatomy Overview	III
Blood Vessels Anatomy Overview	IV
Pulmonary, Systemic, and Coronary Circulation	V
Quantitative Measurements of Cardiovascular System	VI
Introduction to Supplements	IX
Overview of Strength Training/Weightlifting Exercise (anaerobic)	IX
Pre-workout Supplement	XIII
What exactly does this supplement supposedly do for us physiologically?	XVIII
Validity of claims, is this supplement beneficial?	XV
Potential side effects	XVI
Muscle Development Supplement (Creatine-containing)	XVI
What exactly does this supplement supposedly do for us physiologically?	XVII
Validity of claims, is this supplement beneficial?	XVIII
Potential side effects	XVII
Recovery Supplement	XXIII
What exactly does this supplement supposedly do for us physiologically?	XXIV
Validity of claims, is this supplement beneficial?	XXIV
Potential side effects	XXVI
Endurance Exercise (aerobic)	XXVII
Target Audience	XXX
Conclusion	XXXIII
Appendix	XXXIV
References	XXXV

Introduction

It has become essentially common knowledge in the modern era that regular exercise reflects a healthy way of living. Many women and men have chosen the route of exercise that incorporates resistance and free-weights labeled as strength training. Strength-training individuals' goals are to increase muscle size, anaerobic endurance, and muscle strength. Prior studies have found that strength training without supplementation benefits the cardiovascular (CV) system, by several factors including the lowering of an individual's blood pressure as well as increasing Basal Metabolic Rate (BMR).¹²

In today's society it has become a trend to utilize various fitness and exercise supplements to enhance and promote a healthy lifestyle. However, many people do not realize that these supplements have specific effects on the cardiovascular system, and that there are potentially negative effects if used improperly. The supplements to be analyzed in this thesis are ones that are very often used and target strength training/weightlifting exercisers. Dietary supplements for strength training individuals can be categorized into three main categories: Pre-Workout, Muscle Development (During Workout), and Post-Workout supplements. Here we analyze one specific supplement of each category and analyze the supplement's claims, potential benefits, and potential side effects pertaining to the cardiovascular system.

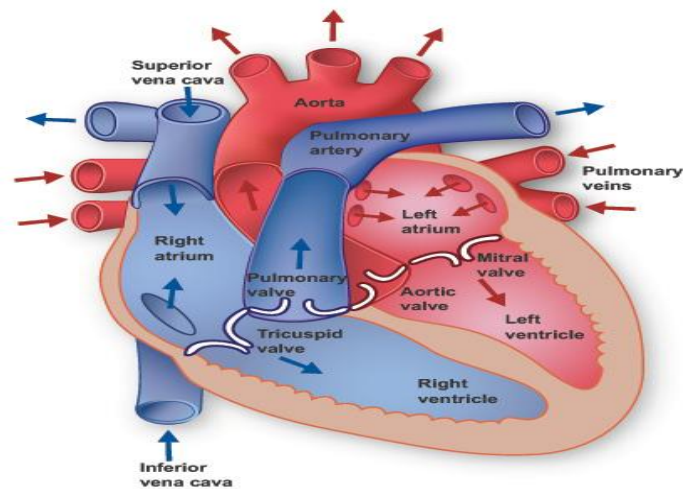
Overview of the Cardiovascular System

The cardiovascular system is composed of the heart, blood, arteries, capillaries, and veins. The anatomy of these constituents is important because it enables us to understand the function of each of these main parts of the system.

Heart Anatomy Overview

The heart is approximately the size of a human's fist and is located within the pericardial cavity of the thorax, anterior to the human vertebral column and posterior to the sternum. The heart is composed of three different layers as follows (from outer to inner): epicardium, myocardium, and endocardium. The epicardium is composed mostly of connective tissue serving as a protective layer for the heart. The myocardium consists of cardiac muscle which allows for the heart to contract and relax, and the endocardium consists of endothelial-like (single layered and flattened) cells that are in contact with the blood pumped by the heart. The whole heart is divided into four chambers that work together to pump blood to the lungs as well as to various tissues, such as muscle, throughout the body. There are two atria that are superior to and supply blood to the two ventricles that are responsible for ejecting blood. The paired right atrium and ventricle are separated by the tricuspid valve while the paired left atrium and ventricle are separated by the mitral (bicuspid) valve. The right ventricle connects to the pulmonary artery via a semilunar valve where blood flows out to the pulmonary circulation system. The right atrium receives deoxygenated blood through the inferior and superior vena cava from the tissues. The left atrium is connected to the pulmonary veins that return blood from the lungs. The left ventricle connects to the aorta via a semilunar valve and ejects blood into the systemic circulation.

Figure 1.0

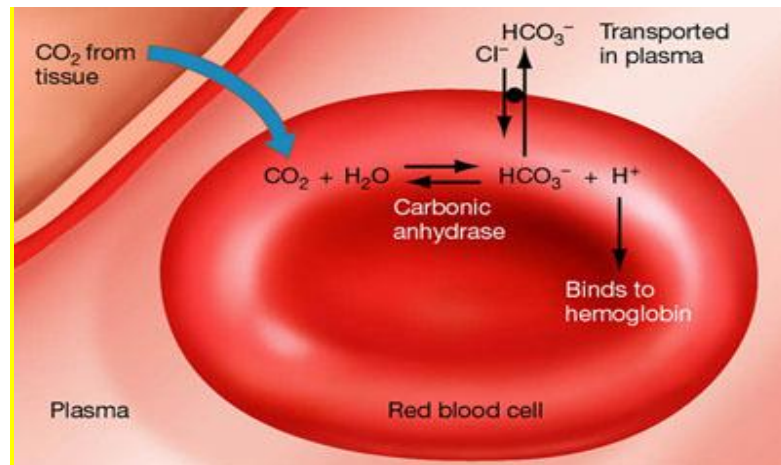


Chambers of the Heart⁶

Blood Anatomy Overview

The substance within the cardiovascular system that allows for oxygen and nutrient transportation throughout the body is the blood. The blood consists of red blood cells, white blood cells, platelets, and plasma. The main cells of interest in the cardiovascular system are the red blood cells since they are the cells that are responsible for oxygen transport. Mature red blood cells lack a nucleus making them flexible which is important so that they may squish through small openings and allow for gas diffusion at the lung capillaries where they are oxygenated. The major molecule within red blood cells, called hemoglobin, contains heme groups which have four iron atoms that are able to temporarily bind to oxygen with a high enough affinity to retain oxygen and a low enough affinity to release oxygen to muscles and tissues in the systemic circulation. Once oxygen is released via diffusion to the tissues that are metabolically active, hemoglobin is then able to bind the waste product, carbon dioxide, and deliver it back to the pulmonary capillaries where it diffuses into the lungs and is exhaled.

Figure 1.1



CO₂ transfer from tissue to red blood cell⁷

Blood Vessels Anatomy Overview

The blood vessels of the cardiovascular system consist primarily of the arteries, veins, and capillaries. The arteries carry blood away from the heart and contain three layers as follows from superficial to deep: tunica externa, tunica media, and tunica intima. The tunica media is the thickest layer consisting of mostly vascular smooth muscle cells. The main arteries in the cardiovascular system are the aorta, carotid artery, subclavian artery, celiac trunk, mesenteric arteries, renal artery, and the iliac artery. The veins of the cardiovascular system are responsible for returning blood to the heart and have the same layers described in the arteries except that veins lack the tunica intima. Generally the veins are much thinner than arteries and they have much less smooth muscle since they are not meant to contract. It's important to note that the veins contain valves that prevent backflow of blood, helping maintain a unidirectional blood flow. Major veins within the cardiovascular system are the subclavian vein, jugular vein, renal vein, and iliac vein. The capillaries of the cardiovascular system are the smallest blood vessels and are essentially the endothelial lining with the thickness of one cell. Their main function is to allow for gas diffusion in the lungs, tissues, and systemic muscles.

In order to understand the function and importance of the cardiovascular system, it is important to address the three circulation systems within it: Pulmonary Circulation, Systemic Circulation, and Coronary Circulation.

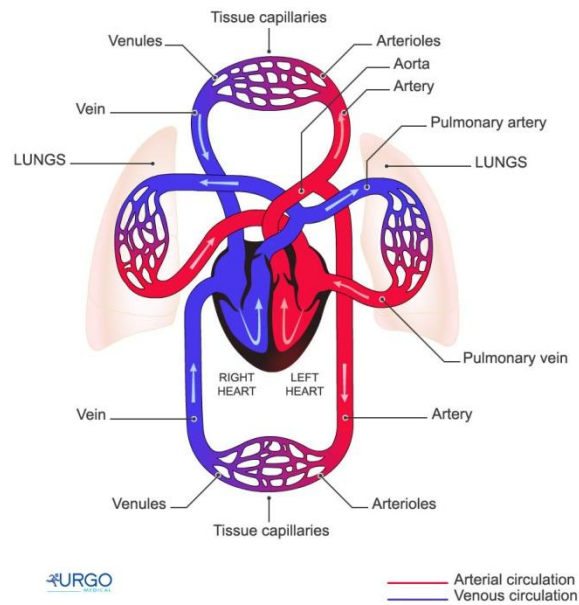
Pulmonary, Systemic, and Coronary Circulation

The Pulmonary Circulation is the segment of the cardiovascular system that distributes oxygen-depleted blood from the heart via the pulmonary artery to the lungs. Deoxygenated blood enters the heart's right atrium via the inferior and superior venae cavae and travels through the tricuspid valve into the right ventricle. Upon right ventricular contraction, the deoxygenated blood flows through the pulmonary semilunar valve into the pulmonary artery. The oxygen-depleted blood moves from the pulmonary capillaries in the lungs where it is oxygenated, and then returns to the heart via the pulmonary vein.

The Systemic Circulation involves the flow of blood from the heart to all parts of the body with emphasis on highly metabolic organs. This particular system drives oxygenated blood away from the heart to parts of the body in need of oxygen in order to function, such as skeletal muscle and tissues. Once blood is pumped to these various regions and oxygen is utilized, the oxygen depleted blood returns to the heart to be pumped back into the pulmonary circulation.

The Coronary Circulation is responsible for providing blood flow to the heart itself, separate from the Pulmonary Circulation. Oxygenated blood flows to the myocardium (heart muscle) via the coronary arteries and deoxygenated blood is carried away from the myocardium via the cardiac veins.

Figure 1.2



Pulmonary and Systemic Circulation⁵

Quantitative Measurements of Cardiovascular System

Understanding the various physics involved with the cardiovascular system is also important in understanding the function of the system and allows for mathematical analysis of blood flow. Calculated values of blood flow that are notable include cardiac output (CO), end systolic and diastolic volume (ESV and EDV), stroke volume (SV), heart rate (HR), and blood pressure (BP). Cardiac output (CO) is described as the rate at which the heart is pumping out blood per minute (measured in Liters/minute). The end-diastolic volume (EDV) is defined as the volume of blood that is pooled into the left ventricle from the left atrium before contraction occurs and has an average value of 135mL^1 . The end-systolic volume (ESV) is the amount of blood that remains in the left ventricle after contraction and seen as an average of 65mL^1 . The stroke volume (SV) is defined as the volume of blood (in ml) that is pumped out of the left ventricle per heart beat. Heart rate (HR) is simply the amount of times the heart beats per minute.

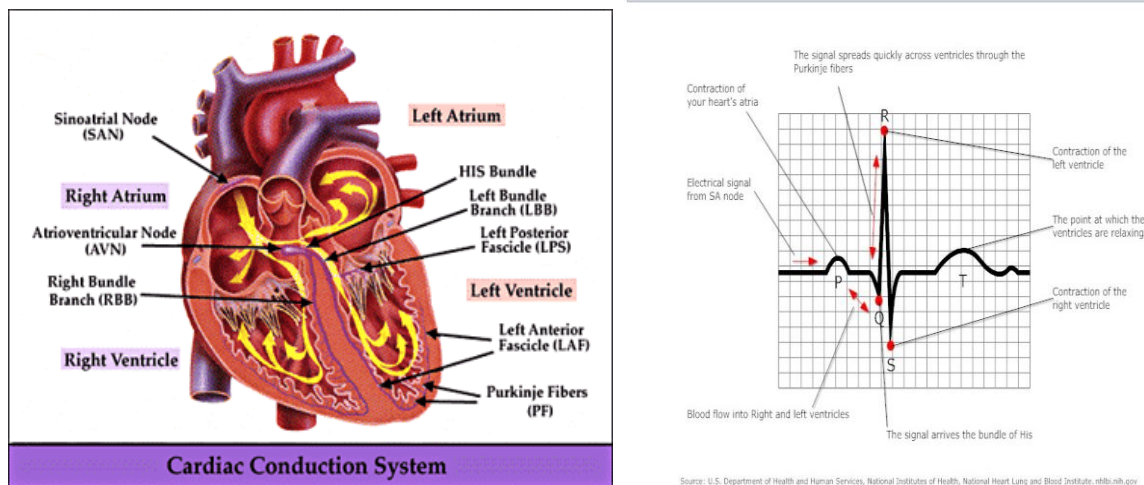
The average untrained human has a general heart rate of 72 beats/min and a stroke volume of approximately 70mL². The blood pressure (BP) is the amount of pressure exerted by circulating blood onto the walls of the blood vessels. Blood pressure is recorded the systolic blood pressure written over the diastolic blood pressure in millimeters of mercury (mm Hg). The average adult blood pressure is approximately 120mm Hg/ 80mm Hg¹.

In order to correlate all the previously described aspects of the cardiovascular circulation system, various equations are used to find the values of each and relationship to each other. The stroke volume is the difference between the end-diastolic volume and end-systolic volume ($EDV - ESV = SV$). Cardiac output is equivalent to the stroke volume multiplied by the heart rate ($CO = SV \times HR$) and is known to have an average value of approximately 5 L/min². It is important to note that the average adult has approximately 5L of blood; therefore approximately the total quantity of blood is circulated throughout the body every minute.

The electrical conduction aspect of the heart explains the way in which electric signals are propagated to allow the heart to continually beat. The heart is considered auto-rhythmic because the sino-atrial (SA) node is able to propagate electric signals on its own without outside stimulation. The heart's electrical conduction system starts with SA node and electric impulse is propagated down to the atrioventricular (AV) node located in the inter-atrial septum close to the tricuspid valve. There is a miniscule delay in time between electric potential movements from the SA node to the AV node to allow for the ventricles to fill with blood. Potential then moves from the Bundle of His and then to the Purkinje fibers in the ventricular walls of the heart. The electrical impulse then stimulates contraction of the muscle of the ventricles' walls causing the pumping of blood out of the heart.

Electrocardiograms (ECG or EKG) are utilized to view the pathway of electric potential throughout the heart. An EKG is viewed as a graph that represents the different parts of stimulation within the heart, with different peaks and troughs marking the key points of electrical conduction. A typical EKG notes the following important parts in a chronological manner: P-wave, Q-R-S complex, and the T-wave. The P-wave represents atrium depolarization and the Q-R-S complex reflects the depolarization of both the left and right ventricles. More specifically, the Q-R-S complex is broken into the Q-wave representing the depolarization of the interventricular septum, the R-wave marks the depolarization of the ventricles, and the S-wave representing downward deflection following the R-wave.³ The T-wave shows the repolarization of the heart's ventricles³. Correlation of an EKG to parts of the heart is shown below.

Figure 1.3, Figure 1.4



To the left, the cardiac conduction system and how it corresponds to an EKG graph on right⁴

Introduction to Supplements

As seen above, the cardiovascular system is a system that needs to be regulated in great detail in order to keep our bodies in homeostasis throughout the duration of our lifetime. In today's society it has become a trend to utilize various fitness and exercise supplements to enhance and promote a healthy lifestyle. Many of these supplements are used nation-wide and even world-wide as people strive to obtain a more healthy and fit image. What many people may not realize is that these supplements might have potential dangers and side effects, specifically within the cardiovascular system, if used improperly. Pre-workout energy, muscle development, and muscle recovery supplementation are three categories that are most commonly utilized. The following provides an example of a popular supplement for each of the mentioned categories with a brief explanation on what exactly they are meant to do physiologically. Before getting into the detailed analysis of these supplements, it is vital to understand what type of exercise they are meant to enhance as well as understand the defining factor of the exercise, strength training.

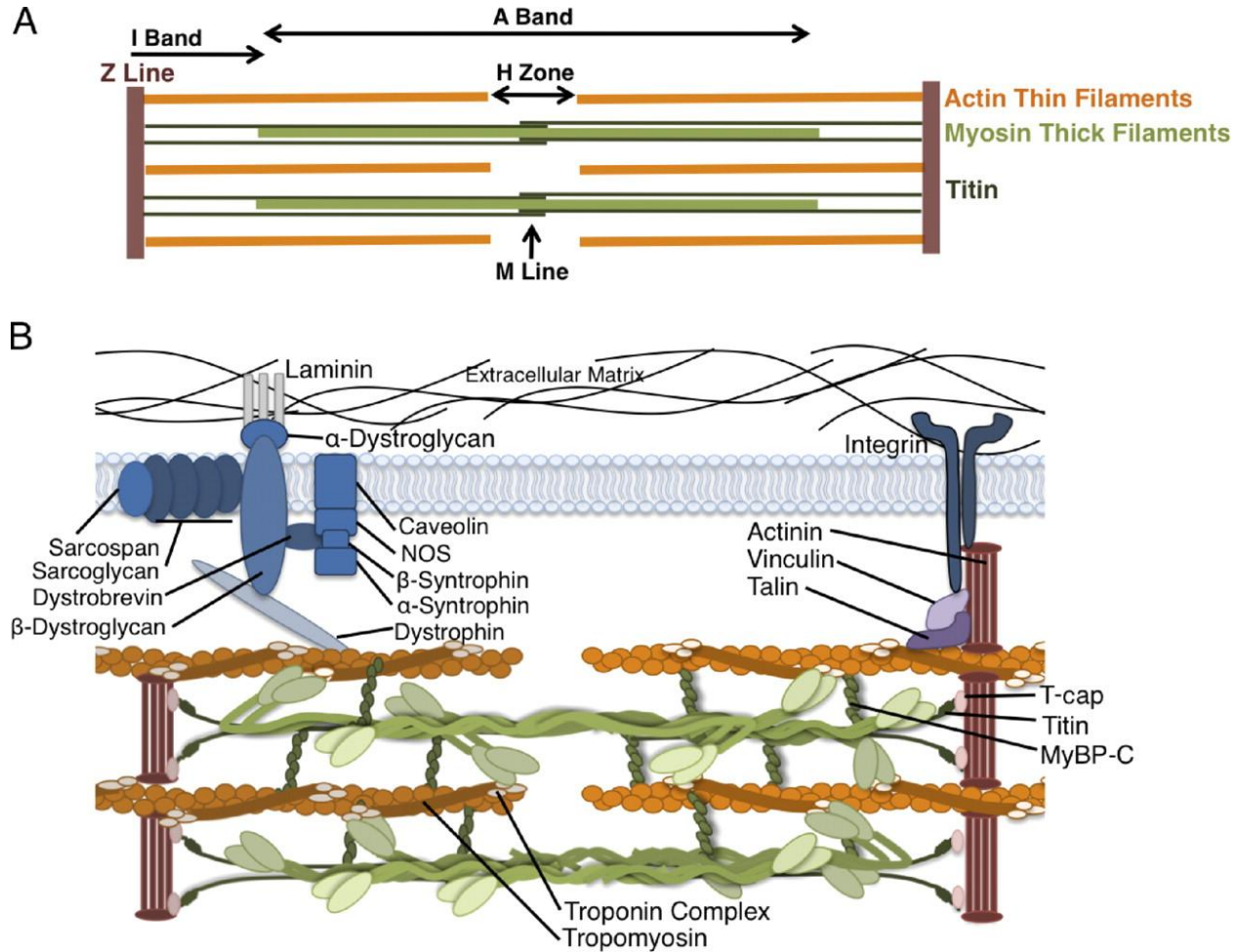
Overview of Strength Training/Weightlifting Exercise (anaerobic)

The particular type of exercise that the analyzed supplements are mostly utilized for are anaerobic exercises, particularly weightlifting. This is commonly referred to a type of resistance training labeled "strength training" in which an individual's goals are to increase muscle size, anaerobic endurance, and muscle strength.⁸ Strength training can be further categorized into two main types depending on the movement involved in the exercise. The first is isotonic exercise which means that the muscle is working against an opposing force such as inertia, momentum, or gravity.¹⁰ Isotonic exercises involve the two main types of training that present day supplements are made to aid; resistance and weight training¹⁰. The second general form of strength training is isometric exercise in which the working muscle group provides an equivalent amount of force to

that opposing it so there is no net movement.¹⁰ For the purposes of analyzing the effects of supplements' physiological effects on the cardiovascular system, isotonic exercise strength training will be the analyzed type of training. More specifically, the "weight training" category of isotonic exercise will be the main focus in terms of its benefits to the cardiovascular system

Weight training is typically done by utilizing the force of gravity and additional weight to provide a force that opposes muscle contraction. In doing this, skeletal muscle is able to increase in strength and size causing hypertrophy of myofibrils in skeletal muscle.⁹ It is relatively important to understand the anatomy of a muscle cell unit when analyzing how weight training can benefit our cardiovascular system. A sarcomere is the basic functional unit of a muscle and is composed of thin filaments called actin, thick filaments called myosin, as well as various proteins and enzymes necessary for contraction.¹¹ For conventional purposes, the sarcomere has various regions of space that constitute the movement of a sarcomere during contraction. The figure below helps to explain the movement involved during contraction.

Figure 1.5: Anatomy of the Cardiac Sarcomere¹¹



“(A) Diagram of the basic organization of the sarcomere. The sarcomere forms the basic contractile unit in the cardiomyocytes of the heart. Thin filaments composed of actin are anchored at the Z line and form transient sliding interactions with thick filaments composed of myosin molecules. The M Line, I Band, and A Band are anatomical features defined by their components (actin, myosin, and cytoskeletal proteins) and appearance in polarized light. Titin connects the Z line with the M line and contributes to the elastic properties and force production of the sarcomere through its extensible region in the I Band. Coordinated shortening of the sarcomere creates contraction of the cardiomyocyte. (B) Representation of the major proteins of the cardiac sarcomere. Attachment to the ECM is mediated by costameres composed of the dystroglycan–glycoprotein complex and the integrin complex. Force transduction and intracellular signaling are coordinated through the costamere. The unique roles of each of these proteins are critical to appropriate function of the heart. T-cap, titin cap; MyBP-C, myosin-binding protein C; NOS, nitric oxide synthase.”¹¹

The benefits weight training has on the human cardiovascular system specifically are seen in the blood component as well as heart tissue. It is important to know the Basal Metabolic Rate (BMR) in humans which is defined as the amount of energy expended per day by humans at rest. Since the act of weight lifting as a re-occurring habit increases general muscle mass, this allows for a correlated increase in BMR, which in turn promotes decreased lipid concentration in the blood.¹² The blood in weight lifting individuals can be seen to impart a lower blood pressure, increased high-density lipid cholesterol (HDL), decreased low-density lipid cholesterol (LDL), decreased triglycerides, and increased GLUT-4 density.¹² This reduces the risk of cardiovascular disease by allowing for less lipid accumulation in blood vessels which reduces the probability of abnormal blood flow due to clotting.¹² These beneficial factors lead to a noticeable increase in cardiovascular factors such as the efficiency of cardiac output (see background pg. 5).

In relation to the benefits in heart tissue, weight training provides evident increases in muscle size, endurance, and strength as earlier mentioned. This relatively small yet healthy amount of hypertrophy in heart tissue in strength training allows for an increased rate of emptying in the heart's left ventricle (although seen more significantly in aerobic cardio exercises).¹³ This leads to a beneficial decrease in the end-systolic volume in the left ventricle (see background pg. 5). Increasing the amount of blood emptying out of the left ventricle then allows for an increase in cardiac output (CO) and hence an increase the tension required by the ventricle to overcome the aortic pressure.¹³ This tension or stress is named "afterload" and is more generally referred to the pressure the ventricle must overcome to eject blood. This beneficial increase in afterload reduces the risk of cardiovascular disease by essentially reducing the energy the heart needs to expend to promote healthy blood flow.¹³

Pre-workout Supplement

1. Cellucor's C4 Extreme

- a. **Claims:** Cellucor's C4 Extreme is a pre-workout supplement that claims to possess "the power to ignite your mind, muscles, and workout regimen." The company Cellucor recommends that C4 Extreme is mixed with water but also mentions that juice can be used as a substitute. This pre-workout supplement has notable active ingredients such as creatine nitrate, beta alanine, arginine AKG, caffeine anhydrous, Vitamin B12, and N-Acetyl-L-Tyrosine.¹⁴

Figure 2.0, Figure 2.1

b. 

30 Servings		Fruit Punch
Serving Size: 1 Scoop (5.9 g)		
Servings Per Container: 30		
Amount Per Serving		% DV
Vitamin C	250 mg	417%
Niacin	30 mg	150%
Folate	250 mcg	62%
Vitamin B12	35 mcg	588%
Beta Alanine	1500 mg	†
Creatine Nitrate	1000 mg	†
Arginine AKG	1000 mg	†
Explosive Energy Blend	718 mg	†
Vitamin C (As Ascorbic Acid), N-Acetyl-L-Tyrosine, Caffeine Anhydrous (135mg), Mucuna Pruriens, Niacinamide, Synephrine HCL, Folate (As Folic Acid), Pyridoxine Phosphate, Vitamin B12 (As Methylcobalamin)		
** Percent Daily Values (% DV) are based on a 2,000 calorie diet.		
† Daily Value not established.		
Other Ingredients:		
Citric Acid, Natural And Artificial Flavors, Silicon Dioxide, Sucralose, FD&C Red Lake No. 40, Acesulfame Potassium (Ace-K)		

Product in selling container to the left and its nutrition facts to the right¹⁴

- c. **What exactly does this supplement supposedly do for us physiologically?** This particular supplement is utilized by exercisers who want a boost of energy before they begin their exercise. It is most commonly used by strength training weight-lifters as it provides energy to skeletal muscle for a more so immediate boost in energy for quick movements as opposed to sustained energy for endurance

exercise. Caffeine anhydrous is simply a form of caffeine that is in powder form and as most people know, is utilized to boost energy and alertness, hence why it is used in this pre-workout supplement. On a relatively intrinsic basis, caffeine works by the mobilization of excess calcium ions from the sarcoplasmic reticulum to remove Troponin C in striated cardiac muscle and induce contraction.

However, a more likely mechanism for this supplement is acting as an antagonist to adenosine which leads to the increase in neurotransmission of neurotransmitters such as acetylcholine, epinephrine, dopamine, serotonin, norepinephrin, and glutamate. All of these neurotransmitters stimulate the central nervous system and therefore provide more energy to skeletal muscles throughout the body. From a physiological standpoint, this increase in the previously mentioned neurotransmitters is known as a positive inotropy, meaning they cause an increase in cytoplasmic calcium in myocardial contractility. This increase in contractility allows for the heart rate to increase as well as stroke volume to increase and therefore leading to an increase in cardiac output.¹⁵ (see background)

- d.** One of the main ingredients that the company Cellucor promotes in their product is creatine nitrate, which has had very little published research conducted on it.

The only viable information found about this product was that a study was conducted at UCLA and found creatine nitrate to be 1000% more soluble compared to creatine monohydrate. Nonetheless, the main incentive behind adding creatine nitrate is to increase calcium levels that creatine provides skeletal muscle and the amino acids (L-arginine and Arginine AKG) to increase the levels of nitric oxide production. This increase leads to vasodilation of blood vessels and

therefore permits greater blood flow to the skeletal muscle advantageously during weight-lifting exercises.¹⁶

- e. **Validity of claims, is this supplement beneficial? Yes and No.** For the most part, the claims made by Cellucor about their pre-workout supplement are correct in terms of stimulation of the central nervous system in order to provide the user with a heightened sense of energy and alertness. This accounts for stimulation due to the ingestion of the following ingredients found in Cellucor: caffeine anhydrous, nitric oxide, and vitamin B12. Although the claims made by the creatine nitrate seem to be correct in terms of its physiological effects as an energy stimulant, there is too little research conducted on this fused compound to verify it. The NO₃ compound that is fused with creatine is commercially known as a vasodilator, causing vasodilation and thus an increased blood and oxygen supply to exercising muscles.¹⁷ However, the supposed mechanism of the amino acids L-Arginine and Arginine AKG leading to an increased nitric oxide amount have been proven to be false.¹⁷ A potential reason for this falsification is that the pH of stomach acid is lower (pH~2.0) than the pK_a of Arginine (pK_a~2.5) and therefore would result in neutralization via protonation of Arginine.¹⁷ This supplementation does not increase plasma concentrations of nitric oxide derivatives. However as an overall stimulant pertaining to the energy provided to the exercising muscle in use, Cellucor's C4 Extreme product seems to be an adequate supplement.¹⁷
- i. Caffeine anhydrous and nitric oxide derivatives are the main stimulant ingredients in this pre-workout supplement, but two other ingredients play

a role that should be considered: Vitamin B-12 and Niacinamide. While both of these B vitamins improve blood circulation and energy supplementation to the brain and central nervous system, it may also cause some potential problems and side effects. Although toxicity has not been posed as a problem for doses of these vitamins in supplements, it should be noted that location-specific injection may not be beneficial.¹⁸

- f. **Potential side effects:** Some major side effects that may occur with this kind of supplementation such as kidney and liver damage and water-retention problems. As most central nervous system stimulants do, Cellucor's C4 pre-workout supplement can cause various side effects such as nervousness, irritability, insomnia, addiction and dependency, heart palpitations and rhythm abnormalities, weight loss, tremors, mild hypertension, hallucinations, convulsions and heart attack. From a cardiovascular standpoint, heart palpitations and dysrhythmia can cause serious concern as they negatively affect normal blood flow, blood pressure, breathing rates, etc.¹⁹

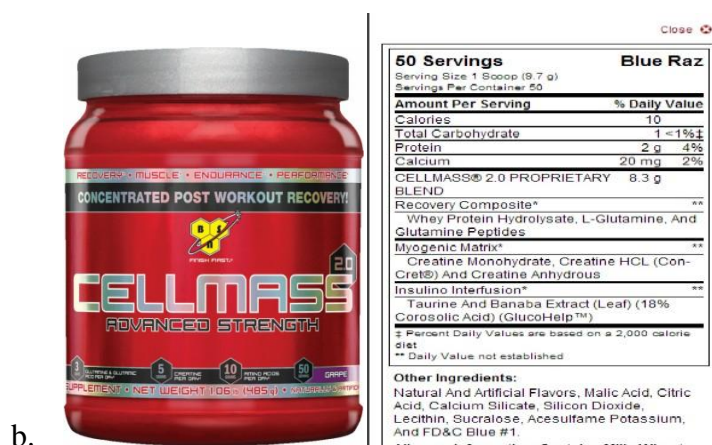
Muscle Development Supplement (Creatine-containing)

2. BSN Cell Mass (concentrated post workout recovery)

- a. **Claims:** This supplement claims to emphasize muscle development and recovery following resistance training. BSN recommends mixing this supplement with water, but also mentions its ability to be soluble in "any beverage of your choice." It contains the following active ingredients: whey protein hydrolysate, L-Glutamine, Taurine and Banaba extract, Creatine HCl (Con-Cret®), Creatine

Monohydrate, and Creatine Anhydrous. BSN claims that Cell Mass advantages include “promoting more efficient recovery, combating muscular fatigue and breakdown, and supports muscle strength, endurance and overall performance.” In addition this supplement contains cinnulin (cinnamon extract) which is claimed to help regulate blood sugar levels.²⁰

Figure 2.2



Product in selling container to the left and its nutrition facts to the right²⁰

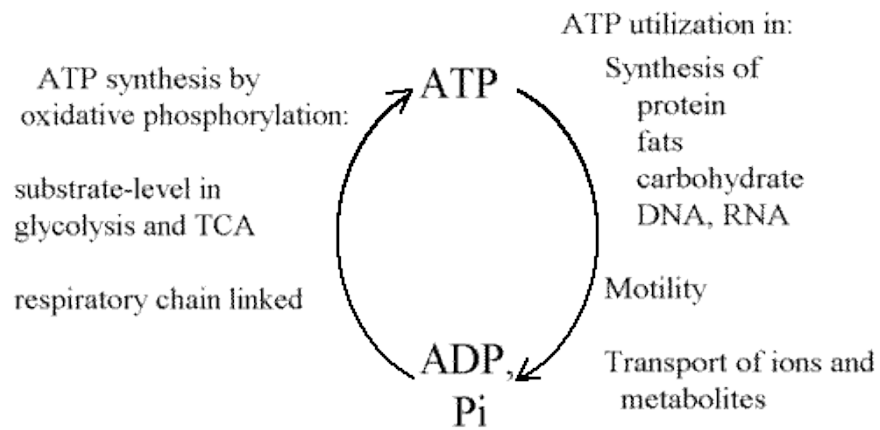
c. What exactly does this supplement supposedly do for us physiologically?

Since protein and amino acids' claims were previously described and proven to be beneficial, the main emphasis for this product will be on the its main ingredient creatine. Creatine comes in three different forms in this supplement, creatine monohydrate, creatine HCL (Con-Cret®), and creatine anhydrous. Creatine monohydrate has been described as the type of creatine that gives weight lifters and athletes increased muscle mass while still retaining muscle tone and leanness. In general, creatine has been seen in various studies to improve performance in strength training weight-lifters in by increasing testosterone, muscle insulin-like

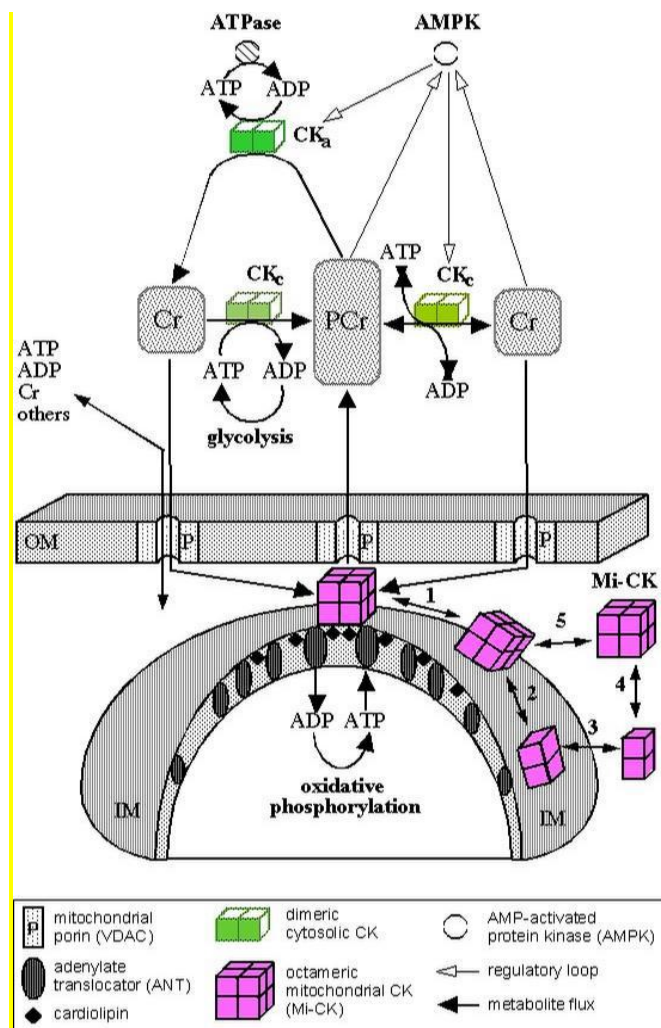
growth factor-I (IGF-I), as well as increasing energy available to the exercised muscles.²¹ The most significant of these increases is the energy available to the muscles being worked.²¹ When used as a supplement, creatine helps to resynthesize ATP from ADP via phosphocreatine (PCr) by utilizing the reversible reaction enhanced by creatine kinase (CK). This allows for an increase in energy supply to the cells that are in high demand of it, specifically skeletal muscle cells for our purposes.

- a. **Validity of claims, is this supplement beneficial? Yes and No.** This supplement's use of creatine in the three various forms described above do indeed increase muscle mass and recovery via the ATP restoration mechanism earlier described. Adenine Triphosphate (ATP) is the energy source utilized by the human body in order for energy-dependent reactions to occur such as muscle contraction. The three phosphate groups attached to the adenine group are the groups that are used as energy sources for cells, muscle cells in this case, when they are broken off one by one by the enzyme ATPase (see Figure 2.1). This verifies the supplement's ability to "promote more efficient recovery, combat muscular fatigue and breakdown, and support muscle strength. In addition, the creatine kinase cycle described above couples with the myosin ATPase cycle in order to regenerate ATP in muscle tissue via phosphocreatine dephosphorylation (see figure 2.2).²²

i. **Figure 2.3**²³



ii. **Figure 2.4**²⁴



- iii. The reason that this supplement does not meet all of its claims from a physiological and cardiovascular standpoint is because there is not significant evidence that it increases exercise endurance. The energy expenditure involved in resistance training while using this product leads to potentially more acute effects involving the ability to resist (lift more) weight, but not exactly effecting the amount of time exercising.²² In addition the potential harmful side effects explained below may play a counter role in its advantages.
- iv. **Additional active ingredients:** An ingredient with unknown function with regards to this supplement is cinnamon extract (anhydrous cinnulin) which has been observed by various clinical studies to reduce sugar (blood glucose) levels.²⁵ Not only was this ingredient found to help in glucose level regulation, it was also noted to play a role in reducing blood pressure and reduce body fat. The concluded mechanism is that the cinnulin reduces fasting blood glucose (FBG) levels by utilizing its bioactive structure (doubly-linked polyphenol type-A polymers) in circulating blood in an unknown detailed mechanism.²⁵ This bioactive cinnulin enhances insulin activity which in turn lowers the FBG and ultimately lowers systolic blood pressure (SBP) by lowering the viscosity of circulating blood.²⁵
1. Currently, cinnamon extract is a highly discussed subject in terms of the health benefits it potentially brings. A study done in 2010 by Beltsville Human Nutrition Research Center in congruence with

the U.S. Department of Agriculture revealed additional benefits to consumption of dietary cinnamon extract. Although the mechanisms behind its benefits are only hypothesized, the study encourages further research on cinnulin's health benefits. Using Wistar rats on a high-fructose diet, the authors were able to obtain results that reflected an increase the mRNA levels that code for adiponectin. Adiponectin is a significant cytokine involved in fatty acid breakdown and regulating glucose levels. Cinnamon extract was also found in this study to inhibit "mRNA and protein levels of fatty acid synthase." This leads to less coding of the fatty acid synthase enzyme, therefore decreasing circulating fatty acid levels. The authors concluded their study strongly suggested that cinnamon extract helps to regulate expression of genes involving insulin sensitivity and lipogenesis in the epididymal adipose tissue, which leads to the "amelioration" of circulating adipokine levels.³⁸ With regards to cinnulin reducing blood glucose levels, the Wistar rats that obtained insulin resistance from a high-fructose diet were supplemented with 50mg/kg of cinnulin. At the end of 8 weeks, the insulin resistance rats obtained noticeably reduced blood glucose, plasma insulin, triglycerides, and total cholesterol levels.³⁸

- v. The second ingredient in this product that goes relatively unnoticed is taurine. Taurine is found naturally in the human body (commonly seen in bile) and is necessary for the function of skeletal muscle as well as

cardiovascular function. When taken in supplementary amounts, as seen in Cell Mass, it has been found to reduce or inhibit oxidative stress that is seen during exercise. Additionally, it has been found to reduce serum lipids as well as increase the efficiency (in terms of force and effectiveness) of heart muscle contractions. These benefits pose potential prevention of coronary heart disease and congestive heart failure, respectively.²⁶

- vi. Another ingredient found in this product that may prove beneficial is banaba extract or *Lagerstoemia speciosa*. The particular compound in the Banaba herb that benefits the cardiovascular system is corosolic acid. Corosolic acid has been found to lower blood glucose levels as well as decrease obesity. A compound in Corosolic acid called “gallotannin” which can both reduce blood sugar as well as inhibit the production of fat cells. An Ohio University study states that Banaba extract may potentially act as an agent for treating diabetes and obesity.²⁷

- d. **Potential Side Effects:** Despite its advantages, there have been numerous cases in which prolonged use or even moderate use has caused kidney problems such as interstitial nephritis, symptoms and/or development of asthma, hydration status, and cramping. This is vital to the effects this supplement has on the cardiovascular system especially in the areas of blood characteristics as well as heart problems. For example, the kidney serves as a regulator of blood pressure by maintaining salt and water balance. Items in this supplement such as creatine monohydrate may lead to the inability of the kidney to regulate water and salt

levels normally and therefore may potentially lead to dehydration, cramping of muscles, and lowered blood pressure. As earlier mentioned, interstitial nephritis in the kidney may possibly occur, a disorder in which inflammation occurs in the space between kidney tubules. This may lead to acute kidney failure that can be noticed by decreased urine output.^{27,28}

- i. The toxicity of taurine should also be considered for potential side effects when utilizing this product. Toxic-level intake of taurine is considered to be around 2g per day which has potential to lead to an autoimmune disease in the skin known as Psoriasis.²⁹


Recovery Supplement

3. Optimum Nutrition's Gold Standard 100% Whey

- a. **Claims:** This particular post-workout recovery supplement claims the ability of “digesting rapidly and is a rich source of amino acids to support muscle recovery.” Optimum Nutrition states this product is highly soluble in water and is the best solvent, however milk and juice are noted to be substitutes that add extra flavor and nutrients. In addition this supplemental source of protein claims to be fast-acting; due to hydrowhey peptides, whey protein microfractions, and Branch Chained Amino Acids (BCAAs) such as Glutamine and Glutamic Acid. The emphasis put on this supplement's claims is that it is easily mixed and “instantized” to mix with a spoon. In addition it offers relatively “low” level of fat, cholesterol, and lactose since the company Optimum Nutrition claims that these are necessities, but in excess is not optimal for the supplement's performance.³⁰

Figure 2.5

b.



5 Lbs.		Double Rich Chocolate	
Serving Size 1 Rounded Scoop (30.4 g)			
Servings Per Container 74			
Amount Per Serving			
Calories		120	
Calories From Fat		10	
		% Daily Value*	
Total Fat	1 g	2%	
Saturated Fat	0.5 g	3%	
Trans Fat	0 g		
Cholesterol	30 mg	10%	
Sodium	130 mg	5%	
Total Carbohydrate	3 g	1%	
Sugars	1 g		
Protein	24 g		
Vitamin A		0%	
Vitamin C		0%	
Calcium		8%	
Iron		2%	
Not a Significant Source of Dietary Fiber			
* Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs.			
Ingredients:			
Protein Blend (Whey Protein Isolate, Cultured Whey Protein Concentrate, Whey Peptides), Cocoa (Processed With Alkali), Artificial Flavors, Lecithin, Acesulfame Potassium, Aminogen®, Lactase.			
ALLERGEN INFORMATION:			
Contains Milk And Soy (Lecithin) Ingredients.			

Product in selling container to the left and its nutrition facts to the right³⁰

c. **What exactly does this supplement supposedly do for us physiologically?** The two main components in this supplement that are noted help muscle building and recovery are whey protein and the amino acid L-Glutamine. Whey protein has been reported to be a main source of muscle development following the stretching of muscles during resistance training. It allows for branched chain amino acids such as valine, leucine, and glutamine to enter the muscle tissue and hence increase the process of enhanced protein turnover. More simply this means that old muscle is degraded and newer, bigger muscle builds.³¹

d. **Validity of claims, is this supplement beneficial?**

i. **Yes.** From a cardiovascular standpoint, this increase in muscle size may allow for stronger muscle built in the heart as well as all systemic muscle tissue that is going through “resistance weight training” or “strength

training” as earlier described (see Overview of Weightlifting Exercise). This means it is possible to increase the physical endurance of an individual and potentially reduce fatigue when training. More specifically, this is caused by an increase in blood pressure (BP) that comes with weight training due to a higher demand in oxygen to the skeletal muscles. The increased BP leads to an increase in afterload due to a higher rate of blood pumped out per beat in the left ventricle. This evident increase in workload endured by the heart leads to increase in cardiac muscle mass labeled as a healthy amount of hypertrophy. Protein and amino acid ingestion following a workout helps to stimulate skeletal muscle protein synthesis. In addition it helps to inhibit muscle protein breakdown following resistance and/or endurance type exercising. It has been noted that the advantages of this protein and/or amino acid consumption is most effective in stimulating muscle protein synthesis when consumed during acute post-exercise recovery.³²

- e. **Additional information:** Notable information on the effects of protein consumption for post-exercise muscle recovery involves two ideas in addition to what was previously mentioned. The first is the amount of protein consumed immediately following a weight training workout. It is now commonly accepted that 20 grams of protein for post-exercise recovery is sufficient enough to obtain maximal protein synthesis rates as it has been successfully included in studies such as the 2011 one conducted by the Maastricht University Medical Center in the Netherlands.³³ This general amount of dietary protein is calculated using

average height and weight for males and females as described in the study.³³ The second notable idea that has been proven to provide the best protein supplementation following weight training is the amount of carbohydrates consumed with the protein. Twice as many grams of carbohydrates (typically glucose or fructose) to grams of protein in a post-workout dietary protein supplement allows for increased muscle hypertrophy and recovery.³⁴ The Exercise Metabolism Research Group at McMaster University in Canada concludes in their 2007 publishing, “We conclude that a small dose (10 g) of whey protein with carbohydrate (21 g) can stimulate a rise in MPS (muscle protein synthesis) after resistance exercise in trained young men that would be supportive of a positive net protein balance, which, over time, would lead to hypertrophy.”³⁴ This is due to a substrate called AS160 that is increased by serum branch-chain amino acids that make up dietary whey protein supplements.³⁵ This substrate induces insulin-induced GLUT-4 translocation and increases insulin-mediated glucose uptake without actually increasing insulin levels.³⁵

- f. **Potential Side Effects:** This product contains two potential allergenic ingredients, milk and soy. Excess protein can lead to possible problems if taken at volumes highly abnormal and often unattainable. As with any consumable product, excess intake of dietary protein may lead to an unnecessarily high caloric intake which leads to accumulation of stored fat. It is possible to potentially develop kidney stones from an extremely high protein diet, but only if the user is not drinking sufficient amounts of water in congruence with the consuming the product.

Endurance Exercise (aerobic)

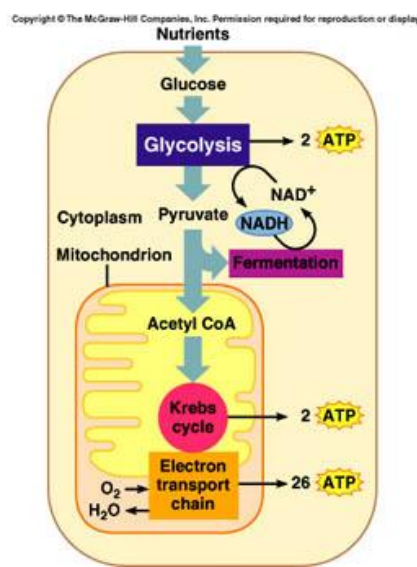
In order to first understand how supplements may potentially aid in performance of aerobic endurance exercise, it is pertinent to know the defining terms of the exercise as well as the physiological benefits it poses for the human cardiovascular system. Aerobic endurance training or exercise entails cardiovascular training where oxygen necessity is determined by energy expenditure. This type of exercise is usually of varying intensity and focuses more on training for an extended period of time that relies on aerobic metabolism. These activities usually include running/jogging, cycling, swimming, walking, hiking, and more for relatively long distances.³⁹

In relevance to the cardiovascular system, aerobic exercise is measured by the functional capacity of the cardiovascular and respiratory system that is termed “aerobic capacity.” Aerobic capacity is also termed $\text{VO}_2 \text{ max}$ (V = volume, O_2 = oxygen, max=maximum) which is short for maximal oxygen consumption. Quantitatively, Fick’s equation is utilized to measure aerobic capacity with the following variables: $\text{VO}_2 \text{ max} = Q (\text{CaO}_2 - \text{CvO}_2)$ where Q = cardiac output (see background), CaO_2 = arterial oxygen amount, and CvO_2 = venous oxygen amount.⁴⁰

The burning question is...how does this exercise benefit humans physiologically? During normal increased muscle exertion, glycogen is broken down via glycolysis, which then produces pyruvate which reacts with oxygen (Citric Acid Cycle in aerobic condition) which results in the formation of carbon dioxide, water, and energy in the form of ATP. In truly aerobic exercise, only carbohydrate forms (such as glycogen) are aerobically transformed into energy, without production of lactate via pyruvate fermentation. Although true aerobic exercise is near impossible to achieve, relatively low-intensity aerobic endurance training is aimed to achieve true aerobic exercise. The major benefit of this exercise is its ability to use glycogen and fat

reserves to fuel activity, resulting in loss of visceral adipose tissue commonly known as the fat amongst the abdomen or the “gut.” During aerobic exercise, muscle glycogen levels begin to decrease causing an increase in glucose released from the liver into the bloodstream. This mechanism coincides with fat metabolism as seen in the figure below. In general, practicing aerobic endurance exercise allows for strengthening in the heart muscle, efficiency cardiac output (see background), reducing resting heart rate, as well as reducing blood pressure (BP, see background). Prolonged aerobic endurance exercise over time leads to the increase in VO_2 max and therefore the ability to endure aerobic exercise for longer time periods. The major performance benefit of aerobic exercise is increasing the amount of energy able to be generated aerobically and hence increases the speed of aerobic metabolism. While this may induce desired fat loss and increased muscle endurance, a set-back of aerobic endurance training would be that it has potential to reduce muscle mass due to its use of both glycogen and fat to produce energy. This reduction in muscle mass is a problem for strength training individuals whose primary goal is to gain muscle mass.⁴¹

Figure 3.0



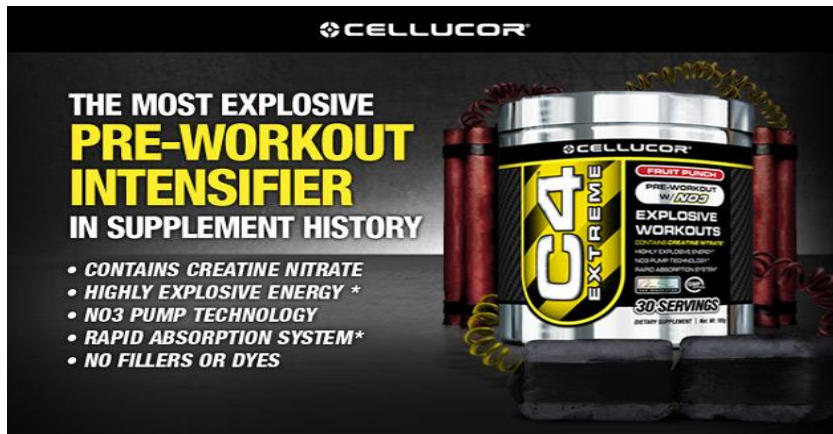
Aerobic respiration in a eukaryotic cell⁴²

While the focus of strength training weight lifting is the primary aim of the types of supplements previously described, aerobic exercise to improve endurance may also benefit from them. Of the three categories of supplementation, (pre-workout, muscle development, post-workout) the post-workout supplementation of whey protein and its branched-chain amino acids (BCAAs) is the only one proven to benefit performance in aerobic endurance exercise. The BCAAs benefit the exerciser after an aerobic exercise by decreasing the net rate of protein degradation, delaying muscle glycogen depletion (when BCAAs taken before and after), and most importantly they decrease the feelings of fatigue.³⁷ The last benefit is the most important because it involves overcoming the feeling of fatigue which is the general goal when doing aerobic endurance training. More specifically, the BCAAs in the whey protein supplement compete with the free tryptophan molecules that are increased during aerobic exercises.³⁷ Normally, the uptake of tryptophan in the brain increases during aerobic exercise, which induces the production of serotonin. Serotonin is thought to play a major role in the feeling of fatigue and therefore increasing its production would lead to the person performing endurance aerobic exercise to experience fatigue.³⁷ BCAAs are transported to the brain via the same carrier system as tryptophan and therefore compete with the tryptophan molecules moving to the brain.³⁷ The brain's decrease in tryptophan uptake allows for a decrease in feelings of fatigue and hence a beneficial increase in aerobic muscle endurance.³⁷

Target Audience

As with almost every commercially sold product, the business market for dietary workout supplements plays a major role in who uses which product and what company is able to thrive in a competitive market. Initially, supplements were advertised for bodybuilders, but as the exponential increase in technological and nutrition advancements continue to occur in society, the common people have become more intrigued with self image and health. Advertisements for the three specific supplements mentioned prior can be found in vitamin shops, nutrition stores, online distributors, and sometimes even at a local convenience store. The claims made by these advertisements are sure to stretch the truth as to what exactly the supplement will do for someone physically and mentally. Unfortunately, supplement companies will provide slogans and/or claims that sound and look appealing to the potential merchant but are not fully true. In general, the target audience ranges from young adults to the elderly, many who are unaware of the science behind these supplements or the potential side effects that they may induce. Evidently there are a vast range of merchants who train regularly and are educated on the potential benefits and disadvantages to taking various types of dietary supplements to enhance performance. For novices attempting to boost their exercising performance, no matter the specific type, purchasing these supplements should be done in a nutritional store with a nutritionist on staff. Consulting a nutritionist to become educated on what exactly a certain supplement is and what it entails is the safest and healthiest way to go about purchasing these supplements. Below are some examples of advertisements found for the three specific supplements previously analyzed for pre-workout, enhanced muscle development, and post-workout recovery in their respective order.

Figure 4.0⁴³



The yellow writing in this add is meant to jump out at the potential buyer with emphasis on the words “Pre-Workout Intensifier.” Adjectives such as “highly explosive,” “rapid,” and “most explosive” give the reader the idea that this is the best pre-workout supplement that will give them energy for the best workout they think possible.

Figure 4.1⁴⁴



This particular ad tries to sway the potential buyer by utilizing the quote “backed by the best” followed by a picture of a body builder with abnormally enlarged back muscles. This is misleading since the portrayed model most likely did not attain his mass by utilization of BSN’s product. In addition BSN highlights the word “best” in the ad in order to have a direct correlation to the red packaging of their product as well as stand out to the viewer to induce the idea that their product is indeed better than others.

Figure 4.2⁴⁵



This ad put together by Optimum nutrition utilizes an extremely lean model in the background in order to emphasize the results that may be possible when using their “world’s best-selling” whey protein. In addition they add two golden ribbons in the picture in order to convince the viewer and potential buyer that their products represents consistent excellence in both results and testing by a popular website that sells nutrition supplements.

Conclusion

After analyzing the three main types of over the counter workout supplements, it was concluded that only the post strength training recovery supplement of 100% whey protein was able to successfully meet all its claims and proved the most beneficial. The pre-workout and during-workout supplements did provide validity for various ingredients, but also had some invalid claims. In addition, it was noted that the effects the latter two had on the cardiovascular system were potentially negative or not necessarily beneficial for strength training exercisers. This review of the cardiovascular (CV) system in congruence with strength training supplements concludes the vital connections between the two are important and should be heavily considered upon use of supplementation resembling any of the three reviewed.

Appendix

Appendix A

"Pumping You Up" The Cardiovascular Effects of Over-the-Counter Weight Lifting Supplements

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Introduction

In today's society it has become a trend to utilize various fitness and exercise supplements to enhance and promote a healthy lifestyle. The supplements to be analyzed in this project are ones that are most often used and target strength training weightlifting exercisers. Strength-training individuals' goals are to increase muscle size, anaerobic endurance, and muscle strength. In terms of strength training's benefits to the cardiovascular (CV) system, it is shown to increase BMR (Basal Metabolic Rate), lower blood pressure, increase high-density lipid cholesterol (HDL), decrease low-density lipid cholesterol (LDL), decrease triglycerides, and increase GLUT-4 density. These factors reduce the risk of cardiovascular disease by allowing for less lipid accumulation in blood vessels which reduces the probability of abnormal blood flow due to clotting. Many people do not realize these supplements' specific effects on the cardiovascular system, and their potential negative effects if used improperly. Dietary supplements for strength training individuals can be categorized into three main categories: Pre-Workout, Muscle Development (During Workout), and Post-Workout supplements. Here we analyze one specific supplement of each category and analyze the supplement's claims, potential benefits, and potential side effects pertaining to the cardiovascular system.

CV System Overview

The cardiovascular system is made up of 5 main components: the heart, blood, arteries, capillaries, and veins. Each component plays a vital role in aerobic strength training and any exercise for that matter. The anatomy of each and characteristics involved in analyzing each one is vital to understanding how strength training supplements affect the system as a whole. Heart (Figure 1) Contains three tissue layers and four chambers (Left Atrium, Left Ventricle, Right Atrium, Right Ventricle). Responsible for pumping blood throughout body. Blood (Figure 2) Consists of red blood cells, white blood cells, platelets, and plasma but main interest is red blood cells since they are responsible for oxygen transport via diffusion. Blood Vessels (Figure 3) Contains three types: Arteries (responsible for carrying blood away from the heart), Veins (responsible for returning blood to the heart and have valves to provide unidirectional flow), and Capillaries (responsible for allowing gas diffusion in the lungs and muscle tissue). All three blood vessels come together to form pulmonary and systemic blood circulation which includes the heart, lungs, and any systemic muscles at work during strength training exercise.

Figure 1.0

Figure 2.0

Figure 3.0

TABLE 1.0 (TERM KEY)	Definition	Equation	Average Value
Blood Pressure (BP)	Amount of pressure exerted by circulating blood on the walls of the blood vessels	$BP = \text{systemic blood pressure} / \text{diastolic blood pressure}$	120 mmHg / 80 mmHg
Blood Volume (BV)	Volume of blood pumped out of the left ventricle per heart beat	$EDV = \text{End Diastolic Volume}$ $ESV = \text{End Systolic Volume}$ $BV = EDV - ESV$	70mL
Heart Rate (HR)	Number of times the heart beats per min.	$HR = \# \text{ of beats} / (1 \text{ minute})$	72 BPM
Cardiac Output (CO)	The rate at which the heart is pumping out blood in liters per min.	$CO = BV \times HR$	5 L/min

Pre-Workout Supplement + its CV effects

Product: Cellucor's C4 Extreme

TABLE 2.0 (MAIN ACTIVE INGREDIENTS)	Caffeine Anhydrous	Creatine Nitrate	Vitamin B12
Physiological Effects	Blocks adenosine, increase neurotransmitters, inc. cytoplasmic $Ca^{2+} \rightarrow$ inc. HR \rightarrow inc. CO	Inc. cytoplasmic $Ca^{2+} \rightarrow$ inc. HR \rightarrow inc. CO	CNS stimulant, inc. ATP to brain
How it helps strength training exercisers	Stimulates CNS, inc. energy (ATP) to skeletal muscles, inc. vasodilation	Inc. vasodilation, inc. blood flow to skeletal muscles	Inc. blood circulation, inc. short term energy

Potential Negative CV effects- nervousness, irritability, insomnia, addiction and dependency, heart palpitations, and rhythm abnormalities, weight loss, tremors, mild hypertension, hallucinations. Heart palpitations and dysrhythmias can cause serious concerns as they negatively affect normal blood flow, blood pressure, breathing rates, etc.

Overall beneficial? YES/NO - This product meets the claim to increase short term energy for strength training exercises as well as increased vasodilation. However its proposed mechanism of increasing NO amounts in blood were disproven.

During-workout Supplement + its CV effects

Product: BSN's Cell Mass

TABLE 3.0 (MAIN ACTIVE INGREDIENTS)	Creatine Mix (monohydrate, HCL, & anhydrous)	Taurine	Banaba Extract (Corosolic Acid)	Cinnulin
Physiological Effects	Inc. testosterone, inc. muscle IGF-1, inc. ATP by re-synthesizing ATP from ADP via PCR by enhancing the reversible an on with OK	Reduce or inhibit oxidative stress caused by strength training, reduce serum lipids, leads to increased blood flow and CO	Decrease circulating blood glucose levels, decrease blood LDL, increase blood flow	Inc. insulin activity \rightarrow dec. FBG \rightarrow dec. BP by lowering the viscosity of circulating blood
How it helps strength training exercisers	Inc. muscle mass (creatine monohydrate), increase energy delivery to muscles, increase testosterone	Inc. blood flow to skeletal muscles in use, inc. efficiency (force and effectiveness) of heart muscle contractions.	Nothing directly, but indirectly has been found to both reduce blood sugar as well as inhibit the production of fat cells.	Increases blood flow to skeletal muscles under stress, and over time lowers BP, allowing for an increase in maximum workload

Potential Negative CV effects- Creatine monohydrate may lead to the inhibition of the kidney to regulate water and salt levels normally and therefore may potentially lead to dehydration, cramping of muscles, and lowered blood pressure. In addition, toxic taurine levels should be considered as the toxic-level intake of taurine is considered to be around 2g per day which has potential to lead to an autoimmune disease in the skin known as Psoriasis.

Overall Beneficial? YES/NO - meets claims to increase muscle mass and recovery via creatine's ATP restoration method, but not claims to improve endurance in strength training exercise.

Post-workout Supplement + its CV effects

Product: Optimum Nutrition's Gold Standard 100% Whey

TABLE 4.0 (MAIN ACTIVE INGREDIENTS)	Whey Protein microfraction + Branch Chain Amino Acids (BCAAs)	L-Glutamine (specific BCAA)
Physiological Effects	Inc. protein turnover, inc. skeletal muscle protein synthesis, causing inc. in CO and max workload	Inc. CO and max workload, inhibits muscle protein breakdown following exercise
How it helps strength training exercisers	Helps to inhibit muscle protein breakdown following resistance and/or endurance type exercising. Old muscle is degraded and newer, bigger muscle built. Increases the physical endurance and reduce fatigue when training.	Increases muscle recovery effectiveness by reducing muscle soreness following strength training.

Potential Negative CV Effects- Excess intake of dietary protein (highly abnormal and often unsustainable) may lead to an unnecessarily high caloric intake, leading to accumulation of stored fat. Possibility to develop kidney stones from an extremely high protein diet, if insufficient water amounts consumed with product.

Overall beneficial? YES-From a cardiovascular standpoint, this increase in muscle mass may allow for stronger muscle built in the heart as well as all systemic muscle tissue that is going through "resistance weight training" or "strength training" as earlier described. This means it is possible to increase the physical endurance of an individual and potentially reduce fatigue when training.

Conclusion

After analyzing the three main types of over the counter workout supplements, it was concluded that only the post strength training recovery supplement of 100% whey protein was able to successfully meet all its claims and proved the most beneficial. The pre-workout and during workout supplements did provide validity for various ingredients, but also had some invalid claims. In addition, it was noted that the effects the latter two had on the cardiovascular system were potentially negative or not necessarily beneficial for strength training exercisers. This review of the cardiovascular (CV) system in congruence with strength training supplements conclude the vital connections between the two are important and should be heavily considered upon use of supplementation resembling any of the three reviewed.

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