

**THE IMPACT OF REGULAR EXERCISE ON ANTIOXIDANTS AND  
SELECTED BIOCHEMICAL HEALTH INDICATORS**

**BY**

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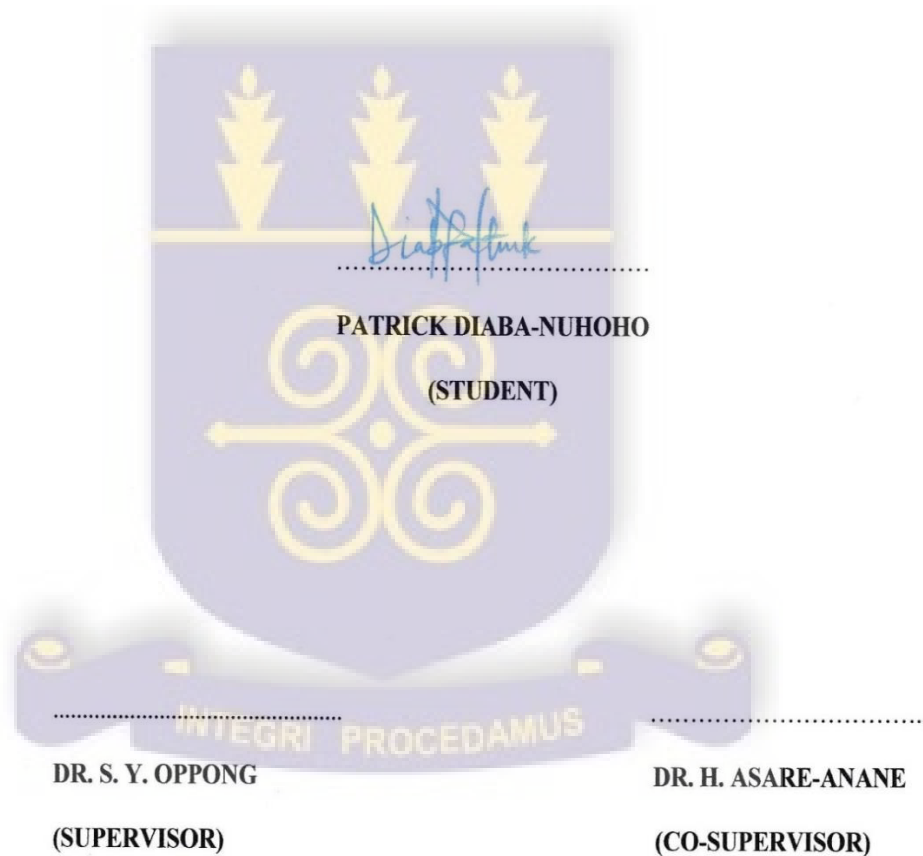
**THIS THESIS IS SUBMITTED TO THE UNIVERSITY OF GHANA, LEGON IN  
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**INTEGRI PROCEDAMUS**

**DECLARATION/SIGNATURE**

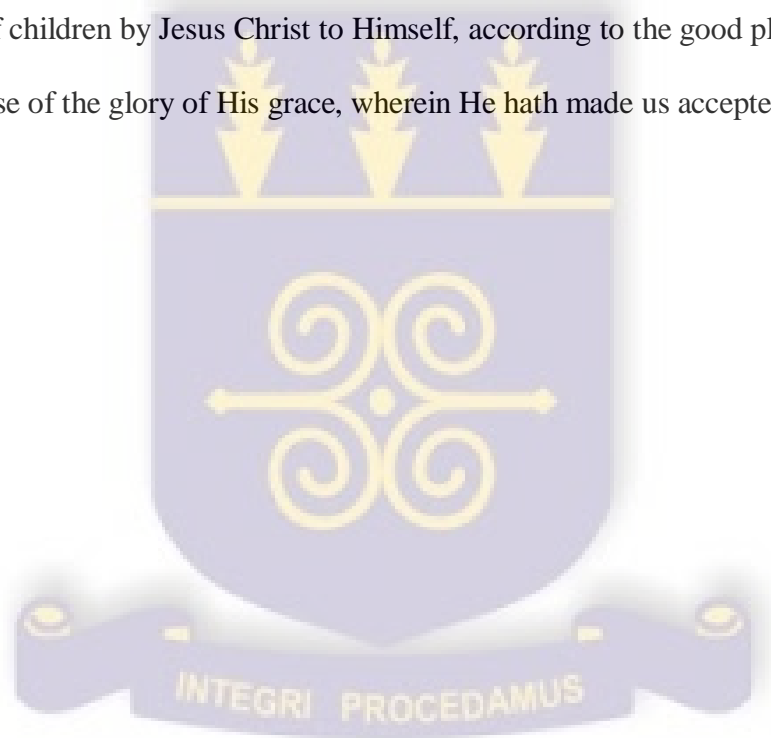
I, Patrick Diaba-Nuhoho declare that this dissertation is the result of my own diligent research work supervised by Dr. S.Y. Oppong and Dr. H. Asare-Anane of the School of Biomedical and Allied Health Sciences, University of Ghana. All references cited in this dissertation have been fully acknowledged.



## DEDICATION

This work is dedicated to Mrs. Sarah Naa Bortey. My course mate who through an untimely death tragedy was taken away from us.

To God be all the glory, awesome thing HE has done. Blessed be the God and Father of our Lord Jesus Christ, who hath blessed us with all spiritual blessings in heavenly places in Christ: According as he hath chosen us in Him before the foundation of the world, that we should be holy and without blame before Him in love: Having pre-destined us unto the adoption of children by Jesus Christ to Himself, according to the good pleasure of His will, To the praise of the glory of His grace, wherein He hath made us accepted in the beloved.



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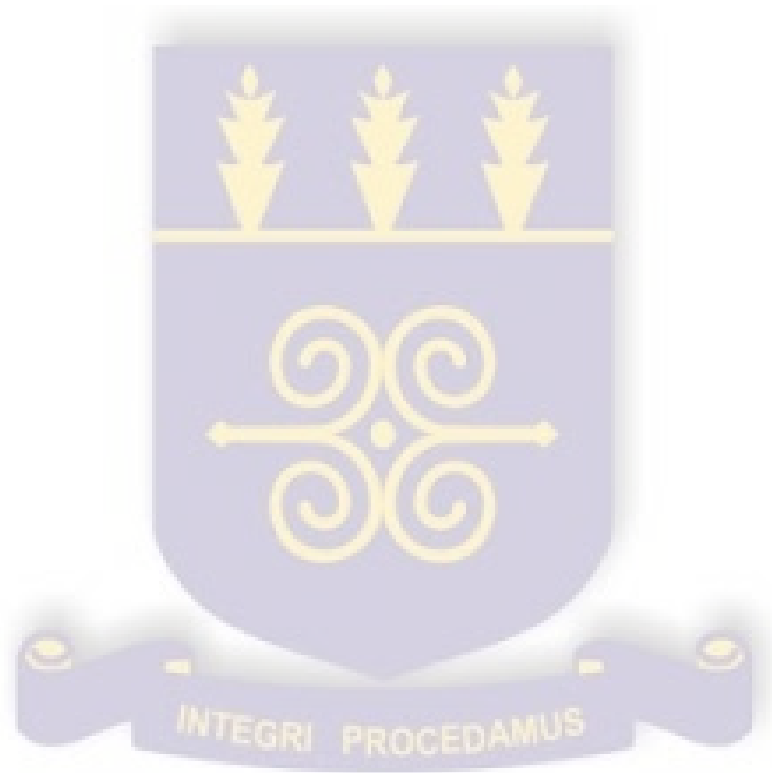
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## ABSTRACT

Intense exercise alters the production of reactive oxygen species (ROS) and may be an effective means to reduce their deleterious effect on the body. Two major classes of endogenous protective mechanisms work together to reduce the harmful effects of oxidants in the cell. The enzymatic scavenging system such as superoxide dismutase and the non-enzymatic antioxidants such as, albumin and uric acid can reduce ROS and protect tissues against oxidative damage. This oxidant-antioxidant balance may affect overall health disrupting changes in biochemical parameters. The purpose of this study was to investigate the effect of regular exercise on circulating antioxidant defences and selected biochemical health indicators in Ghanaian individuals. Eighty-six [44(51.2%) females and 42(48.8%) males] participants with age ranging from 18-59 took part in this study. The exercise group recruited from two gymnasium centres in Greater Accra comprised 42 individuals, made up of 32 (76.2%) and 10 (23.8%) males and females respectively. The control group were 44 in number made up of 9 (20.5%) males and 35(79.5%) females. There was no significant difference in age ( $p = 0.350$ ) between the two groups. An International Physical Activity Questionnaire (IPAQ) that assessed exercise history and demographic characteristics was administered to each participant. Anthropometric measurements (weight, height and body composition) were determined. Biochemical markers (fasting blood sugar (FBS), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides-TG), blood antioxidants markers (superoxide dismutase (SOD) and uric acid (UA) as well as oxidative stress marker (malondialdehyde (MDA) were determined. The mean values ( $p < 0.05$ ) of weight and height showed that the exercise group were heavier and taller compared to controls. The case group also had increased levels in heart rate ( $p < 0.05$ ), daily calorie intake ( $p < 0.05$ ), muscle mass ( $p < 0.05$ ), bone mass ( $p < 0.05$ ) and visceral mass ( $p < 0.05$ ) than the

controls. Oxidative stress MDA and antioxidant SOD markers were significantly higher ( $p < 0.05$ ) in the exercise group compared with controls. Uric acid levels ( $p < 0.05$ ), total cholesterol ( $p < 0.05$ ) and HDL-C ( $p < 0.05$ ) were elevated in the exercise group than the control group and was significant. It is concluded that, participating in both vigorous and moderate regular exercises have some benefits on antioxidant and biochemical parameters compared with mild exercising.



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## LIST OF ABBREVIATIONS

AAP	4-Aminoantipyrine
AD	Anno Domini
ADP	Adenosine diphosphate
ATP	Adenosine triphosphate
BC	Before Christ
BMI	Body Mass Index
CAT	Catalase
CHD	Cardiovascular Disease
CHE	Cholesterol Esterase
CHOD	Cholesterol oxidase
CK	Creatine Kinase
CM	Chylomicron
DBP	Diastolic Blood Pressure
DNA	Deoxyribonucleic acid
FBG	Fasting Blood Glucose
GLUT-4	Glucose Transporter
GOD	Glucose Oxidase
GPX	Glutathione Peroxidase
HDL-C	High Density Lipoprotein Cholesterol
OH <sup>·</sup>	Hydroxyl radical
IDF	International Diabetes Federation
IPAQ	International Physical Activity Questionnaire
LCAT	Lecithin-Cholesterol Acyl Transferase
LDL-C	Low Density Lipoprotein Cholesterol

MDA	Malondialdehyde
MET	Metabolic Equivalent
mRNA	Messenger Ribonucleic acid
NCDs	Non-Communicable Diseases
NHLBI	National Institute of Health, National Heart, Lung and Blood Institute
PEGME	Polyethylene-glycol-methyl Ether
POD	Peroxidase
PUFA	Polyunsaturated Fatty Acid
PVS	Polyvinyl Sulfonic Acid
ROS	Reactive Oxygen Species
SBP	Systolic Blood Pressure
SOD	Superoxide Dismutase
TBARS	Thiobarbituric Acid Reactive Substance
TG	Triglyceride
UA	Uric Acid
VLDL-C	Very Low Density Lipoprotein Cholesterol
WHO	World Health Organization
XO	Xanthine Oxidase

## CHAPTER ONE

### 1.0 INTRODUCTION

#### 1.1 Background

Physical exercise provides a safe and effective means of enhancing and improving quality of life by reducing or preventing side effect of many diseases related to oxidative damages, including cancer (Kushi *et al.*, 2012). Strenuous physical exercise can also cause a rise in the levels of free radicals in the body system, which can result in damage to individual cells. The antioxidant system of these cells can effectively protect these cells against severe damage (Dékány *et al.*, 2008) as the benefits of exercise have long been recognized (Warburton *et al.*, 2006). Regular exercise has the capacity to enhance enzymatic antioxidant defence mechanisms and protect against the impact of oxidative stress (Alessio and Goldfarb, 1988; Radák *et al.*, 2001; Bloomer, 2008). Antioxidants are synthesized naturally by the body (endogenous) and can also be obtained from food (exogenous) such as fruits, vegetables, seeds, nuts, grains, meats, and oil (Diplock *et al.*, 1998; Bouayed and Bohn, 2010). Exercise and antioxidants give protection against diseases such as cataracts, diabetes and cancer (Warburton *et al.*, 2006). Antioxidants are effective because they are willing to give up their own electrons to free radicals. When a free radical gains the electron from an antioxidant, it no longer needs to attack the cell and the chain reaction of oxidation is broken (Dekkers *et al.*, 1996). During the oxidation of polyunsaturated fatty acid, malondialdehyde (MDA) may be formed as a product. This marker of lipid peroxidation can be measured (Esterbauer *et al.*, 1991).

Creatine Kinase (CK), an intramuscular protein, will leak into the serum after membrane damage (Clarkson and Tremblay, 1988). There is evidence that superoxide dismutase protects LDL-C from oxidation (Heinecke *et al.*, 1986). Oxidation of LDL-C is a key

process in the attenuation of atherosclerosis (Steinberg *et al.*, 1989). However, the anion of superoxides can combine with nitric oxide to form peroxynitrite (Blough and Zafiriou, 1985) which is a potent oxidant in the process of atherosclerosis (White *et al.*, 1994). Buttery *et al.*, (1996) also found increased peroxynitrite concentrations in atherosclerotic lesions in humans. Raised serum levels of total cholesterol, triglycerides, LDL-C and VLDL-C has been associated with increased risk of coronary artery disease (Stampfer *et al.*, 1991, Talmud *et al.*, 2002) while conversely HDL-C levels have positive correlation (Lien *et al.*, 1996).

Research by Knez *et al.*, (2014), showed that playing tennis in the heat does not aggravate the development of oxidative stress, but significantly increases antioxidant status and may provide a necessary signal for the up regulation of antioxidant defence, reducing cellular damage. It has been found that regular endurance and resistance training increases the antioxidant defence (Niess *et al.*, 1996; Poulsen *et al.*, 1996) and that two days of strenuous exercise increased the plasma total antioxidant capacity in elite skiers (Subudhi *et al.*, 2001).

The above scenarios suggest exercise and antioxidants may have a positive influence against diseases and will enhance the individual's health and wellbeing. Previous research concerning exercise and antioxidants were done in Asia and European countries with virtually scanty data in Sub-Saharan Africa and Ghana. Also, the fact that this research was based on the life practices and lifestyle of such populations makes it necessary to find out what the situation is like for the people in Ghana. Therefore, the study sought to investigate the effect of regular exercise on circulating antioxidant defences and selected biochemical health indicators such as lipids, fasting blood glucose and uric acid after exercise in Ghanaian individuals.

## 1.2 Problem Statement

There are generalized concerns about the nature of exercise and its health implications. Even though beneficial, a minimum amount of exercise is required for health benefits and beyond a certain level, adverse effects may outweigh benefits (Lee, 2007). Nowadays, a lot of people seem to do all sorts of exercise but the challenge of concern is the increase in free radicals generated during strenuous exercise which may exceed the body's antioxidant defence system. Chronic diseases such as hypertension, obesity, cancer, diabetes and stroke (Amoah *et al.*, 2002; Biritwum *et al.*, 2005 and IDF 2013) are on the rise. Hypertension alone accounts for 4.7% of deaths in Ghana (Ghana Health Service, 2007) with lack of physical exercise contributing to the increase in non-communicable diseases (NCD) (Ministry of Health Ghana, 2007). The World Health Organization (WHO) global status report on NCDs (2014) indicates cardiovascular disease as a major cause of death worldwide with three quarters of those deaths occurring in low and middle income countries. One of the major contributing risk factors is physical inactivity which accounts for 3.2 million deaths annually (Lim *et al.*, 2012). These lead to high cost of management and mortality (Aikins, 2007 and de Graft Aikins *et al.*, 2013), increasing the burden on health care budgets. There is therefore the need for cost effective ways to reduce the incidence of non-communicable diseases and improve health. Even though studies elsewhere (Guillum *et al.*, 1996; Vina, *et al.*, 2012) suggest benefits, the sociocultural and dietary conditions in Ghana may be different and there is a need for evidence-based benefits of exercise in our setting.

### **1.3 Justification**

It is thought that there is a correlation between antioxidant and biochemical health indicators. Exercise is acclaimed to be beneficial to health (Warburten *et al.*, 2006). However, there is a continuous debate on how much, what type, how often, what intensity and how lengthy physical exercise should be. This is important for issuing public health recommendations (Blair *et al.*, 2004). It was thought that a local study such as this one would strengthen the impetus for education aimed at reducing the burden of NCDs which is on the increase (WHO, 2011) as exercise is known to reduce incidence of chronic diseases. It will also help guide the development of policies and programmes to increase activity levels. If found beneficial in this setting it would be an extremely cost-effective way of reducing the cost associated with the management of NCDs. It will also expose individuals who claim to exercise but are not showing health benefits. Furthermore, the study aimed to provide information on the result in Ghana as compared to results from previous studies from other countries, since there is little or no available information on outcomes in Ghana.

### **1.4 Hypotheses**

H: Exercise has no effect on the body's antioxidant defence system and selected biochemical indicators.

### **1.5 Aim**

The aim of this study was to investigate the effect of regular exercise on circulating antioxidant defences and selected biochemical health indicators in Ghanaian individuals.

### **1.6 Specific Objectives**

- To determine the effect of regular exercise on blood antioxidants and selected biochemical markers in Ghanaian adults.
- To determine the relationship between exercise and selected anthropometric characteristics.
- To determine the relationship between antioxidant status and selected biochemical indicators of health.

## CHAPTER TWO

### 2.0 LITERATURE REVIEW

#### 2.1 Exercise

##### 2.1.1 Exercise, Movement and Health

Exercise is a physical activity that maintains physical fitness and optimum health of an individual (Awobajo *et al.*, 2013). There is difference between physical activity (any bodily movement) and exercise [a subset of physical activity that is characterised by a planned and purposeful training (Caspersen *et al.*, 1985)]. The WHO (1946) defines health as ‘Physical, mental, and social well-being, not merely the absence of disease and infirmity’.

##### 2.1.2 Historical Background

In ancient China, as far back as 2500 BC, there are documented accounts of planned exercise for health advancement (Lyons *et al.*, 1978; Lee and Skerrett, 2001). Greco-Roman, 2500 years ago, Hippocrates (460–370 BC) and Galen (AD 129–210) promoted and prescribed exercise for health benefits and stressed the need for care of the athletic individual (Speed and Jaques, 2010). Thus, Plato (427–347 BC) the philosopher said: ‘Lack of activity destroys the good condition of every human being while movement and methodical physical exercise saves and preserves it’ (Fox and Haskell, 1968).

##### 2.1.3 Classification of Exercise

Physical exercises are generally grouped into three types, depending on the overall effect they have on the human body (National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI), 2006). These are aerobic, anaerobic and flexibility exercise. Aerobic or moderate exercise is any physical activity that uses large muscle groups and

causes the body to use more oxygen than it would while resting (NHLBI, 2006). The goal of aerobic exercise is to increase cardiovascular endurance (Wilmore, 2003). Examples of aerobic exercise include cycling, swimming, brisk walking, skipping rope, rowing, hiking, playing tennis, continuous training, and long slow distance training (NHLBI, 2006). Anaerobic exercise is also called strength, vigorous or resistance training and can firm, strengthen, and tone the muscles, as well as improve bone strength, balance, and coordination (NHLBI, 2006). Examples of strength moves are push-ups, lunges, and bicep curls using dumbbells (NHLBI, 2006). Anaerobic exercise also include weight training, functional training, eccentric training, interval training, sprinting and high-intensity interval training that increase short-term muscle strength (NHLBI, 2006; De Vos *et al.*, 2005). Vigorous physical activities are those that take hard physical effort and make a person breathe much harder than normal (IPAQ, 2002). Moderate activities refer to activities that take moderate physical effort and make a person breathe somewhat harder than normal (IPAQ, 2002). Flexibility exercises stretch and lengthen the muscles (NHLBI, 2006). Activities such as stretching help to improve joint flexibility and keep muscles limber (NHLBI, 2006). This helps to better increase movement and reduce injury (NHLBI, 2006; O'Connor *et al.*, 2006).

Metabolic equivalent (MET) is a unit used to estimate the metabolic cost (oxygen consumption) of physical activity. One MET is equivalent to the resting metabolic rate of approximately 1 kcal/kg/h, which is roughly equivalent to the energy cost of sitting quietly. A MET also is defined as oxygen uptake in ml/kg/min with one MET equal to the oxygen cost of sitting quietly, equivalent to 3.5 ml/kg/min. MET-minutes is the rate of energy expenditure expressed as METs per minute multiplied by minutes of a specific activity (Ainsworth *et al.*, 2011).

#### **2.1.4 Exercise and physical activity in Ghana**

A meta-analysis by Abubakari *et al.*, (2009) on fifteen studies published between 1966 and 2007 estimates 13% of West African adults are physically inactive. Low levels of physical activity as well as sedentary behaviour have been found to be associated with mental health problems in Ghana (Asare and Danquah, 2015). A study conducted to find out the effects of social support, stress and health on academic success among Ghanaian adolescents aged 14-21 years revealed that, exercise behaviour such as jogging and participation in physical activity was able to predict and influence academic success in Senior High School students (Glozah, and Pevalin, 2014). In another study to compare gender differences in physical activity among adolescents, boys were more likely to participate in physical activity than girls (Doku *et al.*, 2013) citing culture as the possible influence. Sporting activities are generally perceived to be masculine activities and this makes girls lose interest. Most school children, in the Northern Ghana, Tamale, engaged in moderate to vigorous type of physical activity that showed direct correlation in the type, frequency and duration of activity with age (Mogre *et al.*, 2013). These studies are important as there is suggestion that physical activity levels in children may be a good predictor of the levels of physical activity in adulthood (Dennison *et al.*, 1988).

#### **2.2 Physiological Changes during Exercise**

Exercise results in several physiological changes in the body. The changes occur as a result of long-term exercise program, during or immediately following an activity (Lenz, 2010). During exercise there is increase in blood flow toward working muscles (Lenz, 2010) leaving only 3% of the body's blood to be distributed to the liver and kidneys while 71% of

the body's blood flow during moderate-intensity exercise is received by the muscles (McArdle *et al.*, 1991; Anderson 1968). The redistribution of blood is similar in trained and untrained individuals (Lenz, 2010) but the cardiac output in trained individuals is greater than in untrained individuals during exercise (McArdle *et al.*, 1991).

### **2.3 Health Benefits of Exercise**

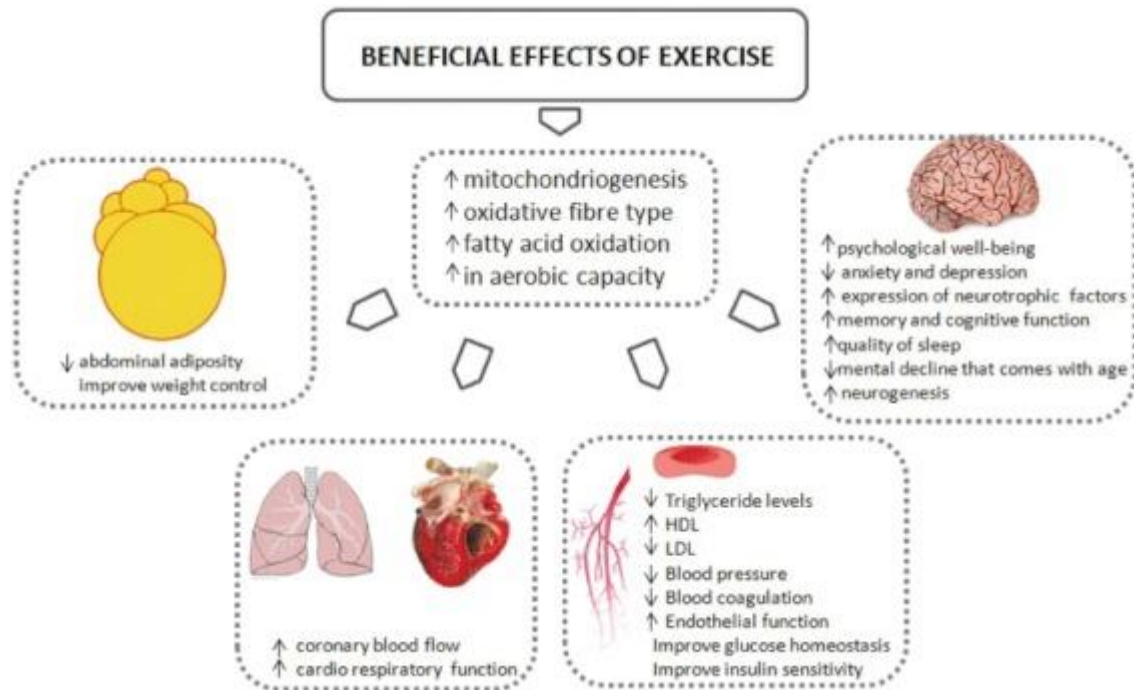
Physical exercise influences and increases the benefits on general health (Warburton *et al.*, 2006). It is one of the most frequently prescribed therapies both in health and disease (Vina *et al.*, 2012) for prevention of pulmonary and cardiovascular diseases such as, chronic obstructive pulmonary disease, hypertension; metabolic disorders involving type 2 diabetes, dyslipidaemia, obesity and insulin resistance; muscle, bone and joint diseases such as rheumatoid arthritis, fibromyalgia, chronic fatigue syndrome and osteoporosis; cancer; and depression (Pedersen and Saltin, 2006; Warburton *et al.*, 2006). Exercise improves self-confidence and self-esteem (Folkins and Sime, 1981). James *et al.*, (1985), showed that physical exercise helps to reduce body weight, enhance glucose metabolism and therefore reduces plasma glucose levels in type 2 diabetes. Despite these benefits, the volume and intensity of the exercise, frequency of administration (sessions per week), type (aerobic vs. resistance exercise) and side effects of the exercise must also be taken into consideration in order to achieve the most benefit from the exercise (Vina *et al.*, 2012). Men and women who have habitual patterns of physical activity and fitness lifestyle have the tendency of reducing their risk of death by about 20%–35% (Blair *et al.*, 1989; Macera *et al.*, 2003).

### 2.3.1 Systemic Adaptations to Exercise

Adaptations to exercise can be seen in the way the cardiorespiratory, musculoskeletal, body composition and metabolic systems function (Warburton *et al.*, 2006; Lee *et al.*, 2010). Exercise training targets the skeletal muscle as it is crucial for enhancing endurance and metabolic efficiency (Matsakas and Narkar, 2010). The exercise improves performance by activating several pathways in skeletal muscle that induce genetic changes to increase aerobic metabolism and vascularization (Narkar *et al.*, 2011). These muscle fibres can be classified as type I slow-twitch or oxidative fibres, with a high mitochondrial content, and type II fast-twitch or glycolytic fibres, which have fewer mitochondria (Vina *et al.*, 2012). These mitochondria are damaged by free radicals and therefore enhance aging (Harman, 1972). Changes that occur as a result of regular physical activity, increase glycogen synthase and hexokinase activities increase messenger ribonucleic acid (mRNA), and protein expression of the glucose transporter GLUT-4 and improvement in muscle capillary density facilitating glucose delivery to the muscle (Mandroukas *et al.*, 1984). Endurance exercise induces an increase in mitochondriogenesis, causing a shift in fibre distribution from glycolytic to oxidative, thereby increasing fatty acid oxidation, inducing rise in aerobic capacity and delays the expression of obesity, type 2 diabetes and cardiovascular diseases (Holloszy and Coyle, 1984; Mootha *et al.*, 2003).

It has been shown that regular exercise can reduce abdominal adiposity and improve weight control (Warburton *et al.*, 2006), enhance lipoprotein profiles (such as reduce triglyceride levels, increase HDL-C and decrease LDL-C levels), improve glucose homeostasis and insulin sensitivity, reduce blood pressure, improve autonomic tone, reduce systemic inflammation; decrease blood coagulation, improve coronary blood flow, augment cardiac function and enhance endothelial function (Warburton *et al.*, 2006). Also,

there is evidence that exercise prescribed as therapy, significantly reduced cancer rates specifically colon and breast cancer in patients (Shephard and Futcher, 1997; Pedersen and Saltin, 2006). Regular physical exercise is also associated with improved psychological well-being through reduced stress, anxiety and depression (Dunn *et al.*, 2001) and cognitive function (Neeper *et al.*, 1995). A possible explanation is the reduction in fat stores, increased energy expenditure from diet, changes in sex hormone levels, immune function, insulin and insulin-like growth factors, free radical generation and direct effects on tumour cell biology during exercise (Westerlind, 2003). Hu *et al.*, (2004) demonstrated a 52% increase in all causes of mortality, a doubling of cardiovascular-related mortality, and a 29% increase in cancer-related mortality in middle-aged women who engaged in less than one hour of exercise per week when compared with regular exercisers. Also less active men who participate in vigorous exercise are more likely to have a myocardial infarction during exercise than the most active men (Thompson *et al.*, 2007). Furthermore, heavy physical exercise triggers the onset of acute myocardial infarction, particularly in people who are habitually sedentary (Mittleman *et al.*, 1993). Correlation between the levels in exercise protocols, training status, age, gender and some biochemical indicators is a frail area and it is known that differences in these levels play a role in oxidant-antioxidant parameters and DNA damage (Sen and Packer, 2000; Yalçın, 1998).



(Adapted from Vina *et al.*, 2012)

Figure 1: The benefits of exercise in the tissues and organs

#### 2.4 Exercise, ROS and Training as an Antioxidant Intervention

Exercise improves cardiovascular health, and also a significant producer of Reactive Oxygen Species (ROS) due to leakage at the mitochondria as a result of increased activity of metabolic process (Davies *et al.*, 1982; Powers and Jackson, 2008). Physical exercise has been reported to increase ROS formation in skeletal muscle (Powers and Jackson, 2008; Ristow *et al.*, 2009) and the magnitude of the exercises can cause an increase in ROS between 2–10%, (Boveris and Chance, 1973) or as high as 10–15% above normal (Alessio, 1993) increasing the free radical production capacity of mitochondria (Ashton *et al.*, 1999; Skarpanska Stejnborn and Szyszka, 2001).

Oxidative stress by mitochondrial oxidative phosphorylation or inflammatory cells leads to the release of oxygen free radicals activating metabolic processes involve in antioxidant

defense systems (Jacob and Burri, 1994). Although, it is not very clear how endurance exercise improves the life span of the body (Ruiz *et al.*, 2011), moderate exercise is a great advantage in cardiovascular benefits (Guillum *et al.*, 1996; Blair, 2009). However, regular exercise has the capacity to enhance enzymatic antioxidant defence mechanisms that protect against the impact of oxidative stress (Alessio and Goldfarb, 1988; Radák *et al.*, 2001; Bloomer, 2008). Exercise increases the expression of antioxidant enzymes (Gomez-Cabrera *et al.*, 2008b) strengthening the body's antioxidant defenses, particularly the glutathione system, which regulate the increased oxidative stress (Leeuwenburgh *et al.*, 1994). This in a way provides a partial explanation for the lower incidence of major diseases and better health of those who undertake regular exercise (Leeuwenburgh and Heinecke, 2001). Exercise in defence system cause redox changes, activate myocardial heat shock proteins, improve myocardiac antioxidant capacity and increase cardioprotective molecules (Ascensão *et al.*, 2007). It is however not known whether the body's natural antioxidant defence system is sufficient to counteract the increase in reactive oxygen species with exercise but, it is known that trained athletes who received antioxidant supplements showed evidence of reduced oxidative stress (Clarkson and Thompson, 2000).

Antioxidant supplements prevent the induction of mitochondrial biogenesis, molecular regulators of insulin sensitivity and endogenous antioxidant defence by physical exercise (Gomez-Cabrera *et al.*, 2008a; Ristow *et al.*, 2009). Thus, reactive oxygen species act as signals in exercise because decreasing their formation prevents activation of important signalling pathways, which cause useful adaptations in cells (Vina *et al.*, 2012).

## 2.5 Biochemical Changes during Exercise

### 2.5.1 Lipid Profile

Exercise has positive impact on the progress, symptoms and physical changes in individuals with elevated cholesterol conferring benefit on their levels (Mann *et al.*, 2014). Exercise enhances the ability of skeletal muscles to utilize lipids reducing plasma lipids (Earnest *et al.*, 2013). Several mechanisms have been hypothesized such as the increase in levels of lecithin-cholesterol acyltransferase (LCAT) which transfers ester to high density lipoprotein cholesterol (Calabresi and Franceshini, 2010) and shown to increase following exercise training (Riedl *et al.*, 2010). Pedersen and Saltin (2006) reported improved levels in the lipid profile following exercise. Aadahl *et al.* (2007) reported physical activity as an intervention for sedentary men and women aged 33 to 64 years. More so, Kesaniemi *et al.*, (2001) noticed a significant improvement in HDL cholesterol after physical activity in his research. Lipid profile describes the different levels of lipids in the blood such as low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) (Mann *et al.*, 2014). Increased levels of LDL cholesterol increases the risk of cardiovascular disease due to the high lipid content in blood. Elevated HDL cholesterol indicates a healthy cardiovascular system (Carroll *et al.*, 2012). Excess TG is independently associated with cardiovascular disease (Luz *et al.*, 2008) and it is obtained from fats eaten in food or other energy sources. Very low-density lipoprotein is correlated to TG and independently associated with cardiovascular risk even with individuals who may have normal LDL cholesterol (Ren *et al.*, 2010). The gold standard for preventing cardiovascular risk is reduced total cholesterol levels (Whayne, 2011) which can be achieved through

continuous aerobic exercise (Epstein, 1995). Thus regular exercise may offer the best means for the reduction in serum total cholesterol levels.

In a review to assess evidence from 13 published investigations and two review articles that addressed the effects of aerobic exercise, resistance training and combined aerobic and resistance training on cholesterol levels and the lipid profile, Mann *et al.*, (2014) confirmed the beneficial effects of regular activity on cholesterol levels and described the impacts of different volumes and intensities of exercise upon different types of cholesterol. Aerobic exercise (60 min, 3 times/week,  $\leq 75\%$  maximum heart rate) improve the LDL-C and TG concentrations. Moreover, a combined exercise of ( $\geq 60$  min,  $> 75\%$  maximum heart rate) also improved the HDL-C concentration (Escalante *et al.*, 2012). Aerobic exercise when performed on regular basis has been shown to improve physical fitness, restore cardiac function, and lower low-density lipoprotein levels, total cholesterol, as well as triglyceride and blood glucose levels (Harris, 1999). Low density lipoprotein constitutes the major transport form of cholesterol in the blood, which carry cholesterol from the liver to the various parts of body. An excess of cholesterol gets deposited in the arteries hence LDL-C is commonly known as bad cholesterol.

In obese men and women who exercised, there was significant change in blood lipid lipoproteins during endurance training (Greene *et al.*, 2012). The body fat increased with increase in serum triglyceride (Hossain-Alizadeh, and Goodarzi, 2014). Schwartz *et al.*, (1992) in their study, to investigate the effect of exercise on young and older men, observed that lipoprotein levels were improved after exercise in both groups. Also, Singh and Sankhla, (2015) found that aerobics may control weight reduction and lipid levels since exercise had a positive impact on weight and lipid profile of subjects and suggested that the inclusion of aerobic exercise in lifestyle practices will reduce the risk factors

associated with diabetes and cardiovascular disease. Conversely, Smoak *et al.*, (1990) after intense physical conditioning of their study subjects observed no change in lipid profile. Equally, a comparative study on exercise and non-exercise groups by Hinkleman and Neiman (1993) observed an increase in HDL-C levels in non-exercise groups and a reduction in exercise group. Suggesting exercise may impact changes on the body.

### **2.5.2 Fasting Blood Glucose**

Increased physical activity improves glucose homeostasis (Wen *et al.*, 2011). It is generally agreed that moderate intensity exercise reduces blood glucose (Jeng *et al.*, 2002; Jeng *et al.*, 2003) although some studies show a greater reduction in glycaemic response in high intensity exercise (Jeng *et al.*, 2003; Hiyane *et al.*, 2008). Human blood glucose concentration is maintained at normal levels during exercise even after fasting despite the depletion of liver glycogen (Dohm *et al.*, 1986). The major determinant of glycaemic changes is exercise volume (Umpierre *et al.*, 2012) while exercise intensity showed a more close association (Boulé *et al.*, 2003). In a study to investigate the effect of different exercise intervention in glucose concentration, there was greater reduction in blood glucose in individuals who exercise (Terada *et al.*, 2013)

### **2.5.3 Antioxidants**

While reactive species are harmful and oxidative stress is dangerous to the body, antioxidants are beneficial and protect against oxidation (Nikolaidis *et al.*, 2012). Antioxidants neutralize free radicals (Sies, 1998) and involve mechanisms, structure or substances that delay, stop, intercept, prevent and remove oxidative molecules (Halliwell

and Gutteridge 2007; Pamplona and Constantini, 2011). Two major classes of intracellular protective mechanisms work together to reduce the harmful effects of oxidants in the cell, the enzymatic and nonenzymatic antioxidants (Dékány *et al.*, 2008). The primary enzymatic antioxidant systems found in cells include superoxide dismutase (SOD), glutathione peroxidase (GPX) and catalase (CAT) (Harman, 1981).

Superoxide dismutase reduces superoxide radical into hydrogen peroxide and molecular oxygen; and catalase and glutathione peroxidase convert hydrogen peroxide into water (Weydert and Cullen, 2009). Also, glutathione peroxidase and other antioxidants such as superoxide dismutase, catalase, and glutathione reductase function to reduce lipid peroxidation (Clarkson and Thompson, 2000). Many non-enzymatic antioxidants also exist in the cell. One member of this family is bilirubin, which is formed by the breakdown of haemoglobin in the spleen, liver and bone marrow and can be found in both the intracellular and extracellular spaces. Bilirubin is capable of protecting albumin-bound fatty acids from lipid peroxidation (Stocker *et al.*, 1984; Stocker *et al.*, 1987).

Endogenous antioxidants can be grouped into complex and simpler molecules. The complex molecules include superoxide dismutase and peroxiredoxins while the simpler ones include uric acid and glutathione (Gutteridge and Halliwell, 2010). Their classification as described by Azzi *et al.*, (2004) and Gutteridge and Halliwell, (2010), is dependent on oxidant ability, neutralization ability and the method used to describe the antioxidant function. Thus they may be classified broadly and functionally into three categories: free radical scavengers such as ascorbic acid; non-free radical scavengers such as catalase and inhibitors of reactive species which includes metal chelators. These antioxidants prevent oxidative stress by inhibiting reactions that would lead to the formation of oxidants, or by scavenging radicals. The defence enzyme, superoxide

dismutase (SOD), takes hold of molecules of superoxide, a particularly destructive free radical and changes them to a much less reactive form. Superoxide dismutase and the glutathione system, work within the cell (Sarma *et al.*, 2010). Circulating biochemicals like uric acid and ceruloplasmin react with free radicals in the intercellular spaces and bloodstream (Sarma *et al.*, 2010).

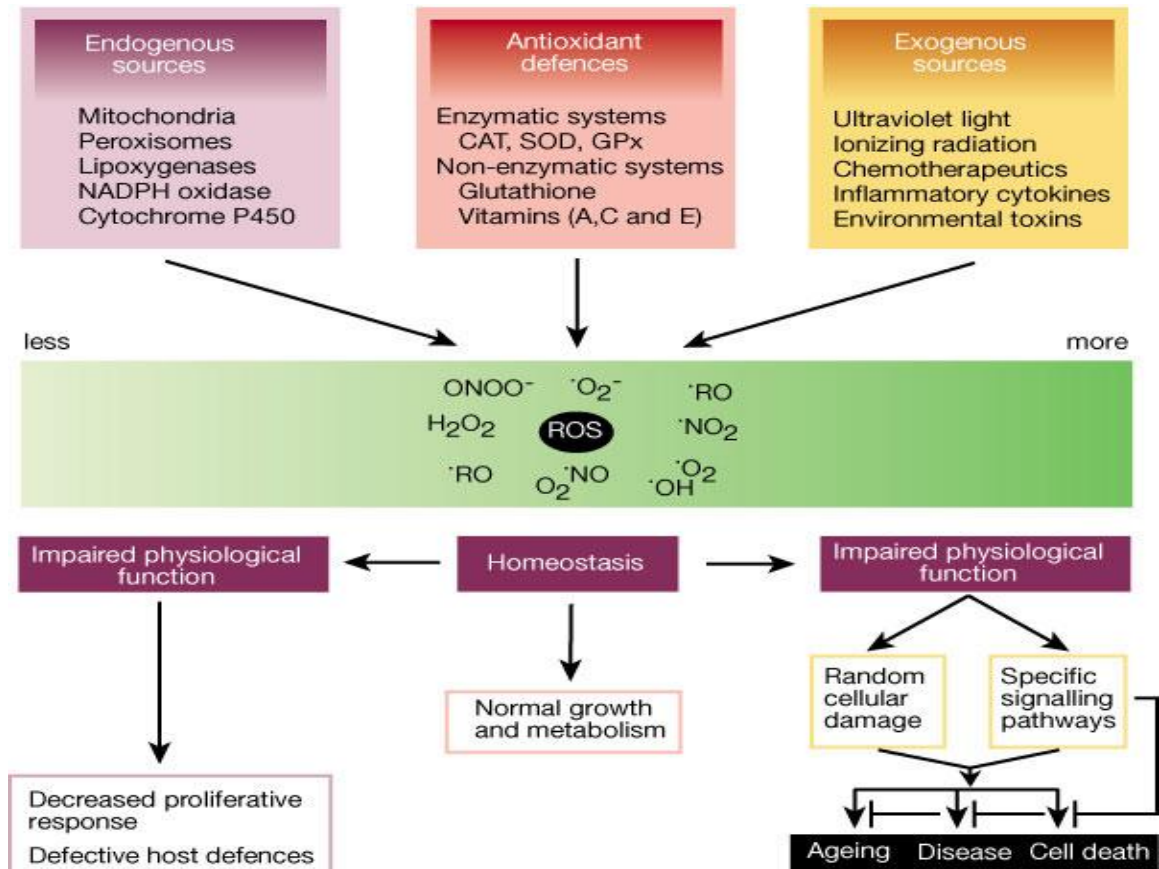


Figure 2: The sources and cellular responses to reactive oxygen species (ROS)

*Oxidants are from normal intracellular metabolism in mitochondria and peroxisomes, as well as from a variety of cytosolic enzyme systems. In addition, a number of external agents can trigger ROS production. Enzymatic and non-enzymatic antioxidant defence system including catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPx) can counteracts and regulate ROS levels to maintain physiological homeostasis. Lowering ROS levels below the homeostatic set point may interrupt the physiological role of oxidants in cellular proliferation and host defence. Similarly, increased ROS may also be detrimental and lead to cell death or an increase in ageing and age-related diseases. Traditionally, the impairment caused by increased ROS is thought to result from random damage to proteins, lipids and DNA. In addition to these effects, a rise in ROS levels may also constitute a stress signal that activates specific redox-sensitive signalling pathways. Once activated, these diverse signalling pathways may have either damaging or potentially protective functions.* (Adapted from Finkel and Holbrook, 2000)

### **2.5.3.1 Antioxidant Supplementation**

Antioxidant supplementation can decrease the extent of free radicals but has not been shown to enhance performance (Clarkson and Thompson, 2000) and while many experiments have suggested benefits of antioxidant supplements such as preventing cancer and heart diseases (Blomhoff, 2005), several large clinical trials have failed to clearly express any advantage. Moreover, excess antioxidant supplementation may be harmful (Ji, 1999). Physical training has been shown to cause a reduction in lipid peroxidation and an increase in antioxidant system because it depends on the intensity of physical activity and the individual training status (Clarkson and Tremblay, 1988). However, Vitamins E and C supplementation of three weeks decreased the malondialdehyde concentration of players who participated in extreme running competition of six long races in the desert (Machefer *et al.*, 2007).

### **2.5.3.2 Uric Acid**

Uric acid is an abundant aqueous antioxidant that accounts for about two-thirds of all free-radical-scavenging activity in human serum (Maxwell *et al.*, 1997). Inhibition of the formation of the hydroxyl radical is considered the most important antioxidant effect of uric acid (Ames *et al.*, 1981). Uric acid itself also reacts with a hydroxyl radical and hypochlorous acid, and inhibits the formation of oxo-heme oxidants (Maples and Mason 1988, Becker *et al.*, 1991). Thus uric acid efficiently inhibits oxidative damage to membranes such as damage by lipid peroxidation and haemolysis (Ames *et al.*, 1993). The antioxidant role of uric acid is in its ability to scavenge carbon-centered and peroxy radicals in hydrophilic states and its inhibitory effect on lipid peroxidation in lipid aqueous

boundary (Muraoka and Miura, 2003). Schlotte *et al.*, (1998) examined if uric acid inhibits oxidation of human low density lipoprotein (LDL) induced by copper and showed that uric acid at concentrations similar to its physiological level can suppress oxidative degradation of LDL components. Uric acid reacts with oxygen-derived from free radicals and becomes oxidized in skeletal muscle during high-intensity exercise (Hellsten *et al.*, 1997). Increased production of oxidative stress due to exercise may lead to high production of uric acid due to DNA degradation and catabolism of purines (Aruoma *et al.*, 1989).

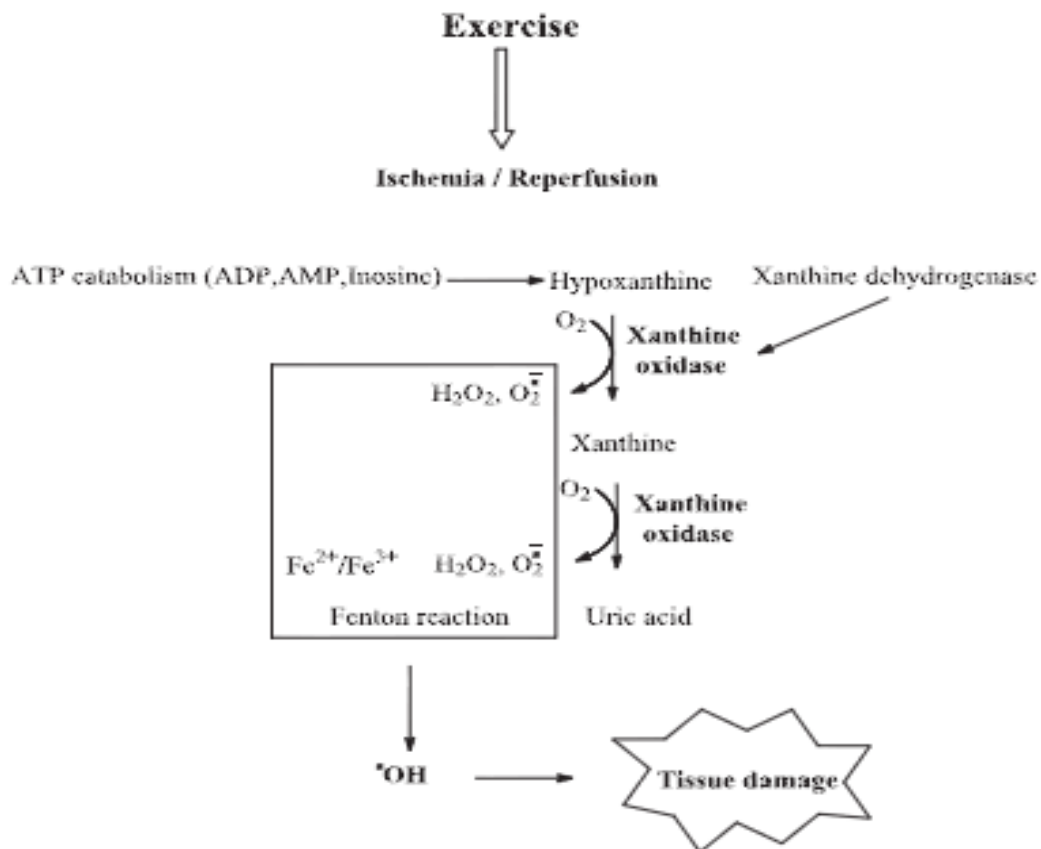


Figure 3: Formation of ROS from Xanthine Oxidase during strenuous exercise

*Under normal physiological conditions XO oxidizes both enzymes hypoxanthine and xanthine to uric acid followed by reduction of NAD<sup>+</sup> to NADH. With intense exercise, under ischemia-like conditions, intercellular levels of XO and hypoxanthine are raised, and*

during reperfusion XO converts hypoxanthine to xanthine and uric acid using molecular oxygen. (Adapted from Kruk, 2011).

Increased production of oxidative stress due to exercise may lead to high production of uric acid due to DNA degradation and catabolism of purines (Aruoma *et al.*, 1989). Intracellular Uric acid concentrations are rapidly replaced by uptake from plasma after exercise (Hellsten *et al.*, 2001). An increase and significant relationship was determined between serum uric acid concentrations and oxidative stress in a study by Mikami *et al.*, (2000) where uric acid concentrations correlated positively with increased serum antioxidant capacity and reduced oxidative stress during acute physical exercise in healthy subjects (Waring *et al.*, 2003). In another study by Huang *et al.*, (2010) it was concluded that serum uric acid increased during vigorous exercise. These suggest that antioxidant properties of uric acid are of biological importance in vivo (Waring *et al.*, 2003) and may arise from purine nucleotide degradation and during conditions of high energy utilization (Green and Fraser, 1988).

#### **2.5.3.3 Malondialdehyde - A Free radical formation**

Fenton reaction (Fenton, 1894) generates Hydrogen Peroxide and Haber Weiss reaction (Haber and Weiss, 1934) generates Superoxide anions which together generate hydroxyl radical (HO<sup>•</sup>), the most reactive free radical produced in biological systems (Bielski and Shiue, 1979). The hydroxyl radical is capable of abstracting methylene hydrogen atoms from polyunsaturated fatty acids (PUFA) to induce lipid peroxidation (Fridovich, 1976). Polyunsaturated fatty acids are large constituents of membrane surrounding cells and organelles such as Arachidonic acid which can undergo several hydrogen removals at

carbons 13, 10 and 7 (Halliwell and Gutteridge, 2007) and because they have double bonds, they are more susceptible to oxidation (Draper *et al.*, 1986; Halliwell and Chirico, 1993). Lipid peroxidation is a process under which oxidants such as free radicals attack lipids containing carbon-carbon double bonds such as polyunsaturated fatty acids (Ayala *et al.*, 2014). Lipid radicals donate electron to oxygen to form a peroxy radical which initiates a chain reaction. This chain reaction is stopped when cyclic peroxide is formed (Figure 4). Fatty acids in the absence of lipid peroxides do not undergo significant peroxidation and lipid peroxides breakdown to release MDA. (Gutteridge and Quinlan, 1983). Lipid peroxidation can cause cell death during oxidative stress (Jenkinson, 1989, Michiels *et al.*, 1994). Malondialdehyde is an end product of polyunsaturated fatty acids and used as a biomarker of oxidative stress (Grune and Berger, 2007). Acute exercise increases ROS production and worsens lipid peroxidation by increasing MDA levels (Kiyici and Kishali, 2012). A study found no effect on serum MDA concentration in resistance-trained and untrained subjects in moderate-intensity whole-body resistance exercise (Dixon *et al.*, 2006). However, regular exercise indicates the strengthening of antioxidant defense (Kiyici and Kishali, 2010).

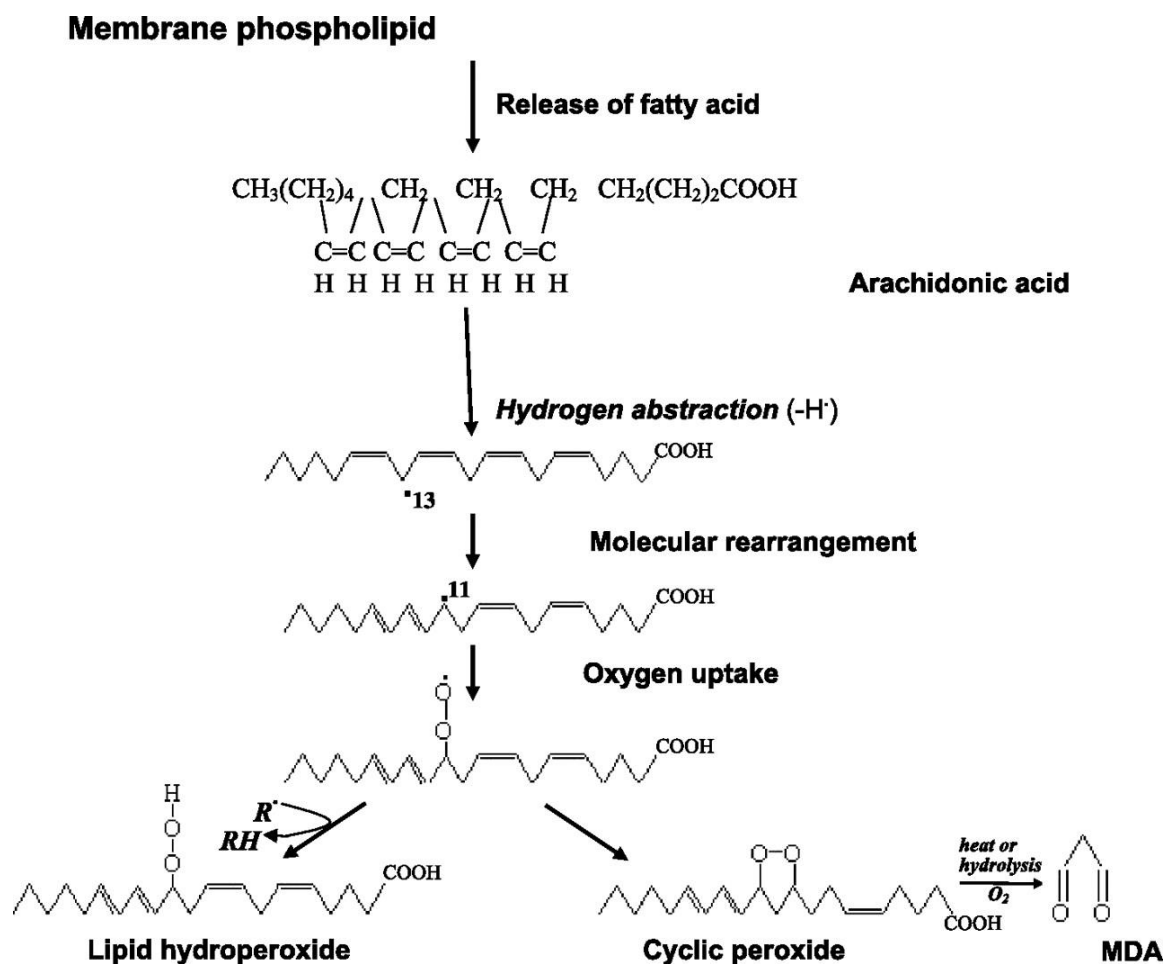


Figure 4: Arachidonic acid undergoing initiation and propagation stages of lipid peroxidation.

(Adapted from Halliwell and Gutteridge, 2007)

#### 2.5.3.4 Superoxide Dismutase

Superoxide dismutase (SOD) catalyses the dismutation of superoxide ( $\text{O}_2^-$ ) into oxygen and hydrogen peroxide and serves as an important antioxidant defense against oxidative stress (Miao and Clair, 2009). Superoxide dismutase is the first antioxidant mobilized by the cell for defence and activates the body's production of its own antioxidants including catalase and glutathione peroxidase (Skarpanska-Stejnborn *et al.*, 2011). There are three forms of SOD (Figure 5); namely, cytoplasmic superoxide dismutase (SOD1),

mitochondrial superoxide dismutase (SOD2), and extracellular superoxide dismutase (SOD3) present in mammals (Miao and Clair, 2009). Superoxide dismutase (SOD1) (Copper zinc superoxide dismutase (CuZn-SOD) is found in the cytoplasm and organelles of virtually all mammalian cells (Liou *et al.*, 1993). Superoxide dismutase (SOD2) (Manganese superoxide dismutase (MnSOD) is found in the mitochondria of almost all cells (Weisiger, and Fridovich, 1973). Superoxide dismutase (SOD3) (Extracellular superoxide dismutase (EC-SOD) is a secretory copper and zinc containing SOD distinct from the CuZn-SOD (Marklund, 1982). Extracellular superoxide dismutase is synthesised by only a few cell types, including fibroblasts and endothelial cells, and is expressed on the cell surface where it is bound to heparan sulphates. Extracellular superoxide dismutase is the major SOD detectable in extracellular fluids and is released into the circulation from the surface of vascular endothelium following the injection of heparin (Karlsson *et al.*, 1993). Extracellular superoxide dismutase plays a role in the regulation of vascular tone, because endothelial derived relaxing factor (nitric oxide or a closely related compound) is neutralised in the plasma by superoxide (McIntyre *et al.*, 1999). Hitomi *et al.*, (2008) examined the effect of acute exercise on the expression of SOD and showed that the expression of extracellular SOD (EC-SOD) increased significantly in skeletal muscle whereas no change was observed for cytoplasmic and mitochondrial SOD.

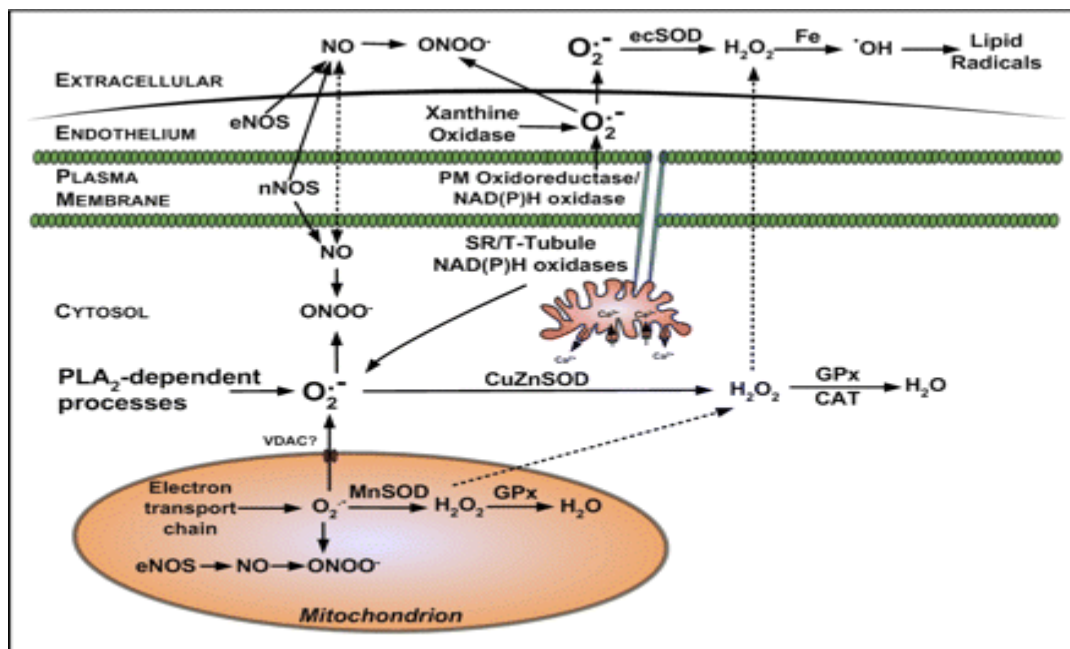


Figure 5: Potential sites for the production of superoxide in skeletal muscle.

*Skeletal muscle generates superoxide at multiple subcellular sites, several of which increase in activity during muscle contractions. Numerous potential sites for superoxide production exist in skeletal muscle and are summarized in the following segments. (Adapted from Powers and Jackson, 2008)*

## 2.6 Effect of Exercise on Body Composition, Body Weight and Blood Pressure

Body composition is the relative proportion of fats and lean meat (bones, tissues, organs and muscle) in the body (Esmat, 2012). Body composition within recommended range suggest an individual has less risk of developing obesity related diseases such as diabetes, high blood pressure and cancers (Esmat, 2012). Thus regular physical exercise reduces the risk of developing obesity (Farrell *et al.*, 1998). A 3-year combined exercise program on body composition and lipid profile in elderly women induced positive adaptation in body composition and lipid profile in elderly women (Kosmidou *et al.*, 2014). Active lifestyle, influence energy balance and body fats when exercise is done on a regular bases. This

suggests exercise and body weight may have some correlation (Chaput *et al.*, 2011). Exercise without weight loss is associated with increase in skeletal muscle mass (Ross and Janiszewski, 2008). In a cross-sectional study of physical activity and obesity, it was found that physical activity was inversely associated with Body Mass Index (BMI) (Besson *et al.*, 2009). In individuals who were hypertensive, weight training exercise maintained the reduction in blood pressure and endurance training elicited further reduction in blood pressure (Hagberg *et al.*, 1984). This reduction in blood pressure was recently confirmed in a meta-analysis to examine the effects of various exercises on resting blood pressure in adults by Cornelissen and Smart (2013). It was discovered that endurance, dynamic resistance and isometric resistance training lowers systolic blood pressure (SBP) and diastolic blood pressure (DBP).

## **CHAPTER THREE**

### **3.0 SUBJECTS AND METHODS**

#### **3.1 STUDY SITE AND STUDY DESIGN**

This was a cross-sectional study. Sedentary controls were administrative staff in the various departments of the College of Health Sciences, University of Ghana. Control subjects were recruited if they participated in less than 1 hour of planned activity each week. Two selected gymnasium centres in Greater Accra Region were used for this study. The gymnasium centres were the University of Ghana sports Directorate and Yok 250 at Mamprobi. Eighty-six participants were recruited into the study. Forty-two exercise individuals and forty-four controls.

#### **3.2 SAMPLING POPULATION AND TECHNIQUE**

The subjects were selected from the two study sites in the Greater Accra Region. Participants were consecutively selected from each gymnasium site. The objective of the study was thoroughly explained to the participants and those consented and fulfilled the inclusion criteria were enrolled into the study. A random sampling technique was used in the selection of participants.

##### **3.2.1 Inclusion Criteria**

- Apparently healthy individuals 18 - 59 years of age
- Individuals willing to sign informed consent
- Those who normally undertook moderate to intense exercise (subjects were included if they undertook at least three formal exercises for 30 minutes per session at their gymnasium centres each week).

### **3.2.2 Exclusion Criteria**

- Subjects who smoked or had any chronic illnesses like obesity, hypertension and diabetes.
- Pregnant and lactating mothers.
- Those on vitamin and antioxidant prescriptions.
- Failure to sign informed consent
- Subjects who used herbal supplements
- Subjects who exercised less than 3 times per week and less than 30 minutes per session.

### **3.2.3 Exercise Programme**

Exercise intensity and duration was quantified (minutes/week) using the International Physical Activity Questionnaire (IPAQ, 2002) (Short, self-administered format) (Booth, 2000). The IPAQ consist of 4 questions that determine the subject's average amount of vigorous and moderate exercise, as well as the amount of walking and sitting they do each day. Exercise had to be at least 10 min of continuous activity to be recorded. Vigorous exercise was classified as intensities similar to jogging, heavy lifting, digging, aerobics, or fast cycling. Moderate physical activity was classified as exercise intensities equivalent to carrying light loads, cycling at a regular pace, or doubles tennis. The walking category included walking at work, at home, to travel from place to place, for recreation, sport, exercise, or leisure. Sitting included sitting at a desk or table, visiting friends, reading, travelling, and watching television.

### 3.3 SAMPLE SIZE

A sample size of 73 was determined based on an absolute precision of 5% and a confidence interval of 95%, in agreement with the strategic function of Epiinfo Statistical Software used. Allowance was given for a non-participation rate of 10% and non-response rate of 20%.

$$N = \frac{(z)^2 (SD) (1-SD)}{E^2}$$

$$= \frac{1.96^2 (0.05) (0.95)}{0.05^2}$$

$$= 72.9904$$

Where N is estimated sample size

E is desired margin of error

Z is the critical Z score on the desired level of confidence (95%)

SD is the standard deviation

### 3.4 DATA COLLECTION AND ANTHROPOMETRIC MEASUREMENT

#### 3.4.1 Data Collection Tools

Data were collected using a validated interviewer-administered questionnaire (Appendix III). A structured interview form was administered to the consented participants during the data collection. The questionnaire, was in English, and rendered in the local language as required.

#### 3.4.2 Height

Height measurements were taken using a Seca Stadiometer (SEC-213, Birmingham, United Kingdom) with the head of the individual being assessed standing erect without

support with head in a Frankfurt plane, knees and legs together and bare foot. The height measurements were taken to the nearest 0.1cm.

### **3.4.3 Body Composition**

Weight was measured using a Seca 770 floor digital scale to the nearest 0.1kg with subjects in minimal clothing. BMI was computed as (weight [kg] / (height<sup>2</sup> [m<sup>2</sup>])). A Tanita innerscan<sup>TM</sup> body composition monitor (BC-533, UK) was used to obtain weight, body mass index (BMI), percentage body fat, body water percentage, muscle mass, bone mass and visceral fat readings with the individual standing erect without support, bare foot and in minimal or light clothing. The range for classification of BMI into categories was based on the World Health Organization criteria (2003) for adults. The range was defined as underweight < 18.5(kg/m<sup>2</sup>), normal weight 18.5-24.5(kg/m<sup>2</sup>), overweight 25-29.9 (kg/m<sup>2</sup>), obese 30 (kg/m<sup>2</sup>).

### **3.4.4 Blood Pressure and Pulse Measurement**

An Omron Digital Blood Pressure 705 CP oscillometric monitor (Kyoto, japan) was used to measure the blood pressure and pulse after participants were allowed to have a fifteen minute rest. The arm of a participant was relaxed on a hold-up at a height approximately at the heart level and participants were asked to sit quietly. The cuff of the monitor was wrapped around the left fore-arm just 1-2 cm above the elbow with the participant in a relaxed position. Blood pressure and pulse measurements were checked three times at five minutes intervals. These precautions were observed to minimize measurement errors and to reduce bias of a single measurement. The mean of the three measurements was used for the analysis.

### **3.5 SAMPLE COLLECTION AND LABORATORY TESTS**

#### **3.5.1 Blood sample collection**

After about 10-12 hours overnight fasting, five millilitres of venous blood was drawn by a trained phlebotomist. Three millilitres of blood was put into a gel separator tube and centrifuged at 1000 rpm for 10 minutes after clotting and the sera obtained was aliquot in 1ml portions into two sterile Eppendorf tubes, one for antioxidant measurements and another for lipid profile analysis. Two millilitres of the blood was placed in a fluoride-oxalate tube for glucose estimation. Plasma was separated from cells by centrifugation at 3000 rpm for 10 minutes. All samples were labelled and stored at -20°C until use.

### **3.6 BIOCHEMICAL AND ANTIOXIDANT ANALYSIS**

#### **3.6.1 Lipid and Antioxidant Analysis**

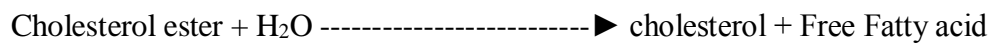
Kits for the estimation of total cholesterol (TC) and triglyceride (TG) were purchased from Medsource Ozone Biomedicals Pvt, Ltd, India and kits for HDL-C and LDL-C were purchased from JAS Diagnostics, Inc., Florida. Assay kits for superoxide dismutase (SOD) and malondialdehyde (MDA) were purchased from Bioassays systems, USA and that of Uric acid, from JAS Diagnostics, Inc., Florida. The lipids and uric acid were analysed using Biotechnica BT-3000 plus chemistry Analyser (Rome, Italy) following manufacturer's instructions. Enzymatic determinations of absorbance at specific wavelength were measured at 37°C. All protocols were followed using manufacturer's instructions.

### 3.6.1.1 Total Cholesterol Test Principle

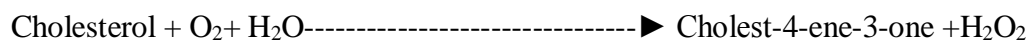
Cholesterol esterase catalyses the hydrolysis of cholesterol esters to produce free cholesterol in serum sample. Together with pre-existing free cholesterol, they are oxidized in a reaction catalysed by cholesterol oxidase to form cholest-4-ene-3-one and hydrogen peroxide in the presence of water and oxygen.

In the presence of cholesterol oxidase (CHOD), the hydrogen peroxide formed is used to oxidize 4-aminoantipyrine (AAP) and phenol to produce a red quinoneimine complex that is read at 505 nm. The absorbance measured is directly proportional to the total cholesterol concentration. The equations summarising the sequence of reactions is shown below:

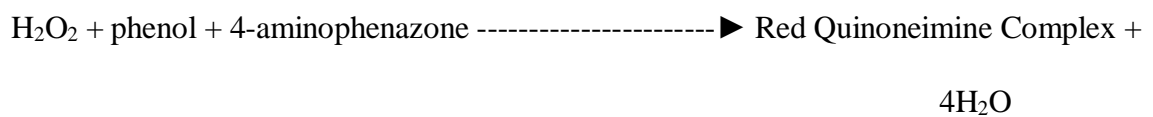
Cholesterol esterase (CHE)



Cholesterol Oxidase (CHOD)

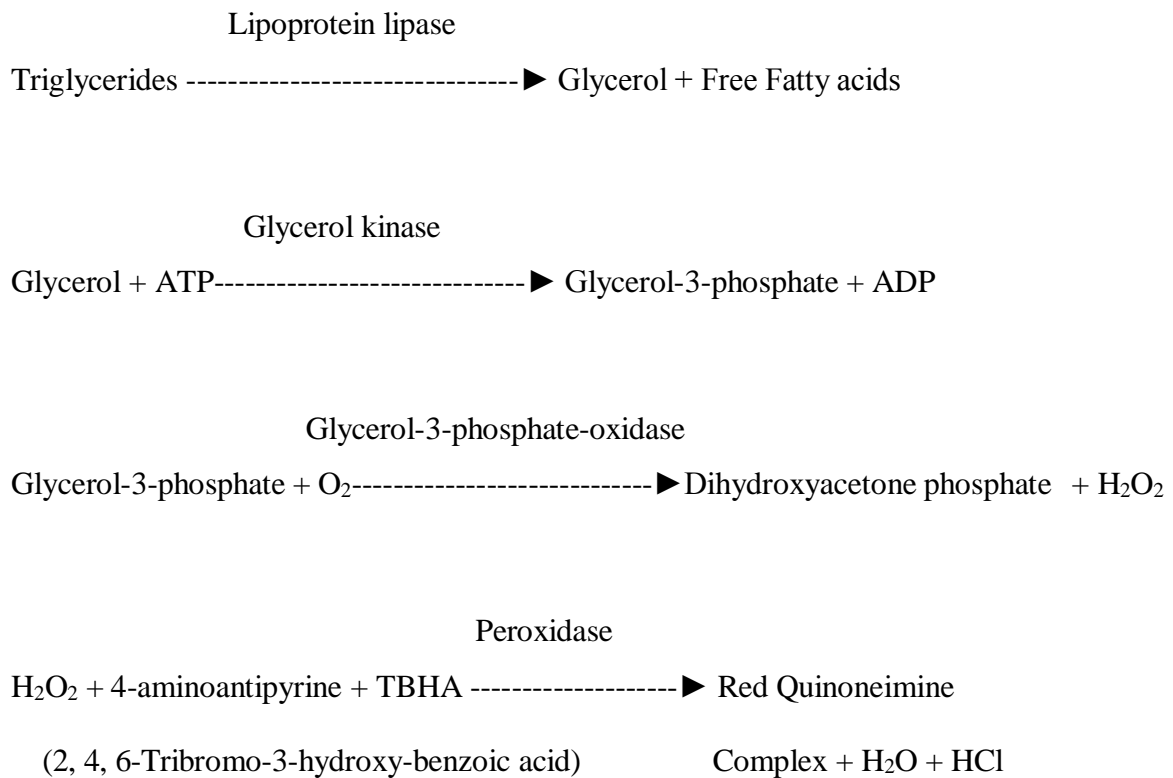


Peroxidase (POD)



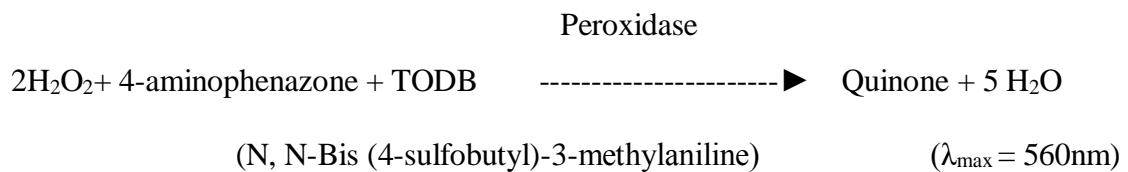
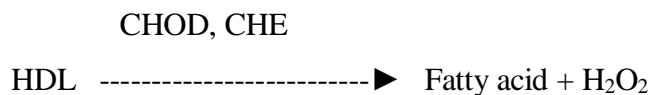
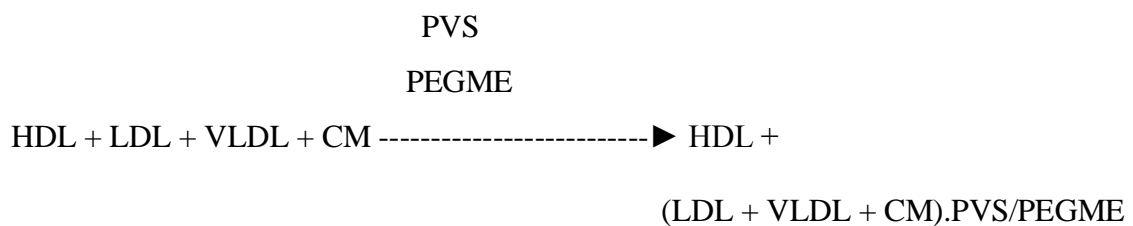
### 3.6.1.2 Triglyceride Test Principle

The triglycerides present in serum are catabolised into glycerol and free fatty acids by lipoprotein lipase. Liberated glycerol is converted to glycerol-3-phosphate in the presence of glycerol kinase and ATP. Glycerol-3-phosphate was acted upon by glycerol-3-phosphate oxidase to form hydrogen peroxide. This together with the phenolic compound TBHA and 4-Aminoantipyrine in the presence of peroxidase gives a red colour complex. The intensity of the colour measured at 505nm is proportional to the triglycerides concentration.



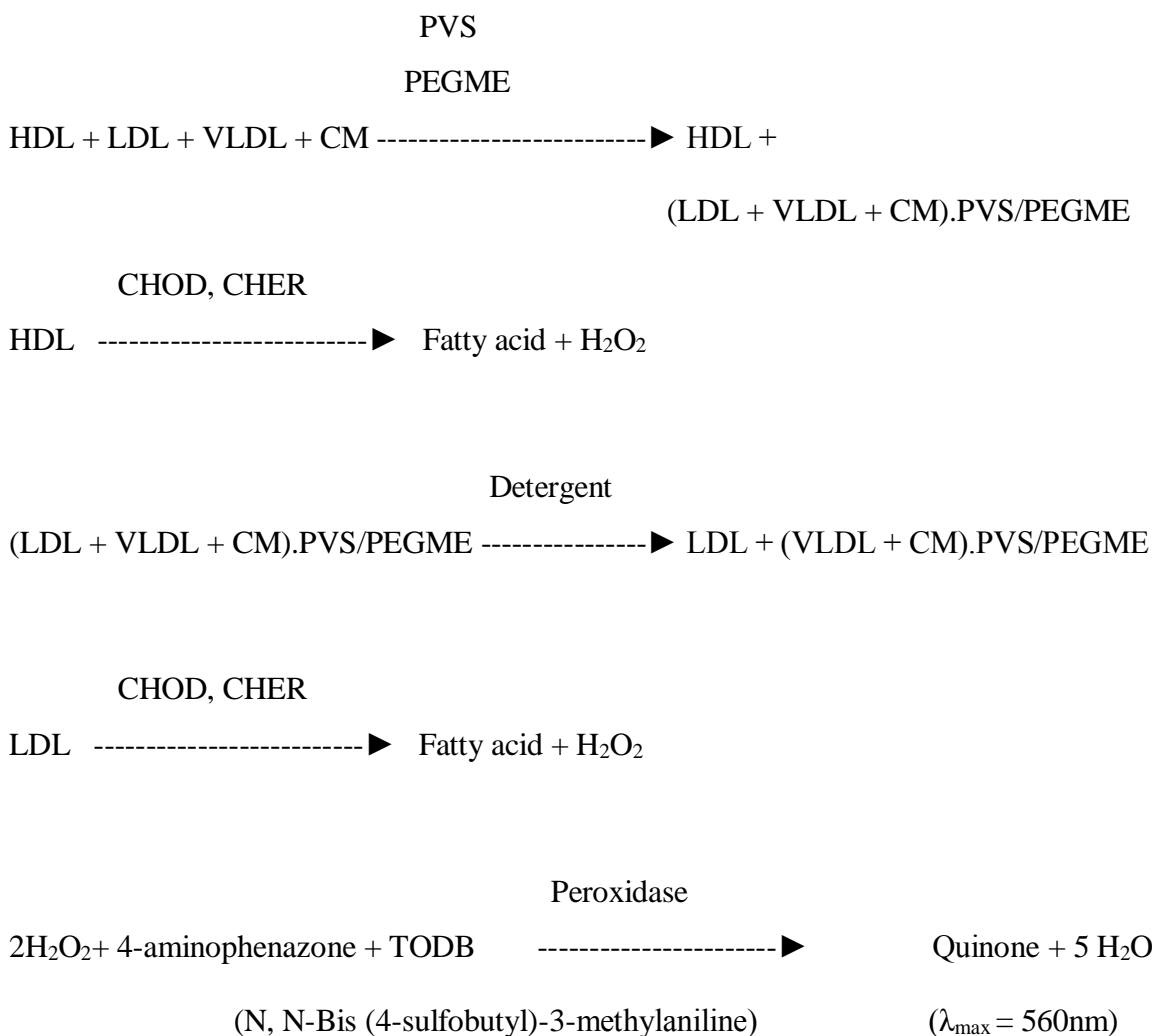
### 3.6.1.3 HDL- Cholesterol Test Principle

The assay is based on a modified polyvinyl sulfonic acid (PVS) and polyethylene-glycol-methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PVS/PEGME and selected detergents (Xiao, 2002). LDL, VLDL, and chylomicron (CM) reacts with PVS and PEGME and the reaction results in the inaccessibility of LDL, very low density lipoprotein cholesterol (VLDL-C) and CM by cholesterol oxidase (CHOD) and cholesterol esterase (CHE). The enzymes selectively react with HDL to produce H<sub>2</sub>O<sub>2</sub> which is detected through a Trinder reaction.



### 3.6.1.4 LDL- Cholesterol Test Principle

The assay was based on a modified polyvinyl sulfonic acid (PVS) and polyethylene-glycol-methyl ether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PVS/PEGME and selected detergents (Xiao, 2002). LDL, VLDL, and chylomicron (CM) reacted with PVS and PEGME and the reaction resulted in the inaccessibility of LDL, VLDL and chylomicron (CM) by cholesterol oxidase (CHOD) and cholesterol esterase (CHE), whereas HDL reacted with the enzymes. Addition of R2 containing a specific detergent released LDL from the PVS/PEGME complex. The released LDL reacted with the enzymes to produce H<sub>2</sub>O<sub>2</sub> which was quantified by the Trinder reaction.



### 3.6.1.5 Very Low Density Lipoprotein Cholesterol Test Principle

Concentration of VLDL was evaluated as the triglyceride concentration/2.2.

$$[\text{VLDL}] = [\text{TG}]/2.2$$

### 3.6.2 Glucose (Fasting Blood Glucose) Analysis

Fasting blood glucose concentration was estimated using liquizone glucose (GOD-POD) kits purchased from Medsource Ozone Biomedicals Pvt, Ltd, India and analysed using Biotechnica BT-3000 plus chemistry Analyser (Rome-Italy) following manufacturer's protocol. Glucose present in serum was oxidized by the enzyme glucose oxidase (GOD) to gluconic acid with the liberation of hydrogen peroxide, which was converted to water and oxygen by the enzyme peroxidase (POD). 4-aminoantipyrine. An oxygen acceptor took up the oxygen and together with phenol formed a pink coloured chromogen which was measured at 505 nm.



### 3.6.3 Superoxide Dismutase Analysis

BioAssay Systems' SOD assay provides a convenient colorimetric means for the quantitative determination of SOD enzyme activity in biological samples. In the assay, superoxide ( $\text{O}_2^-$ ) was generated by xanthine oxidase (XO) catalysed reaction.  $\text{O}_2^-$  reacted with a WST-1 dye to form a coloured product. Superoxide dismutase scavenged the  $\text{O}_2^-$

thus making less  $O_2^-$  available for the chromogenic reaction. The colour intensity ( $OD_{440nm}$ ) was used to determine the SOD activity in a sample.

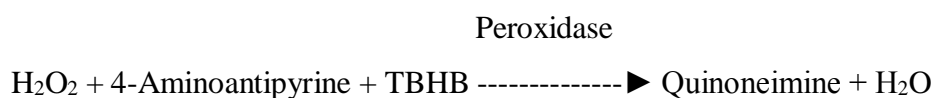
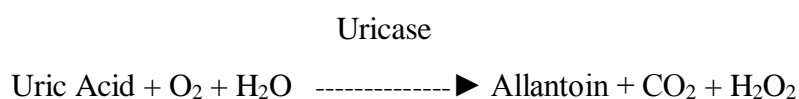
### 3.6.4 Malondialdehyde Analysis

Malondialdehyde levels were determined based on BioAssay Systems' thiobarbituric acid reactive substances (TBARS) assay (Volpi and Tarugi, 1998; Ashton *et al.*, 1999; Clarkson *et al.*, 2000).

Samples were heated with thiobarbituric acid (TBA) to form a pink coloured product. After cooling, the coloured products were extracted. A standard of known concentration was run alongside the tests. The protocol from bioassay Systems was used and the colour intensity at 535 nm was measured spectrophotometrically using a flat plate ELISA reader.

### 3.6.5 Uric Acid Analysis

Serum uric acid (mmol/L) was oxidised by uricase allantoin and hydrogen peroxide. Tert-butyl hydroperoxidase (TBHB) + 4-aminoantipyrine + hydrogen peroxide, in the presence of peroxidase, produced a quinoneimine dye that was measured at 520 nm. The colour intensity at 520 nm and at 37°C was proportional to the concentration of uric acid in the sample.



### **3.7 DATA MANAGEMENT AND STATISTICAL ANALYSIS**

The data obtained through the questionnaires was entered into the computer using Microsoft® Excel® software. Using the Ainsworth *et al.*, (2011) compendium of the average MET score for each type of activity, the following values were used for the analysis of IPAQ data: walking at work = 3.3 METs, moderate intensity = 4.0 METs and vigorous intensity = 8.0 METs (IPAQ). Analysis of data was done using a statistical package for social scientists (SPSS), version 20.0. Physical activity scores and levels were calculated according to the guidelines for data processing and analysis of the IPAQ. Continuous scores were expressed as MET-minutes per week (MET level × minutes of activity/day × days per week) (IPAQ). One-way analysis of variance (ANOVA) was used to compare differences in groups. Where a significant difference was observed using the one-way ANOVA, post-hoc unpaired t-tests was used to evaluate differences within groups. The data was reported as mean ± standard error of the mean. Statistical significance will be set at  $P < 0.05$ .

### **3.8 ETHICAL ISSUES**

Permission from the Ethical and Protocol Review Committee University of Ghana Medical School College of Health Sciences was sought regarding this research. Permission was obtained from the authorities of the gymnasiums before start of the project. An informed written consent was sort from the participants before allowing them to partake in the research. Confidentiality of participants was ensured at all times. Right to withdraw from the study at any time by participants was not hindered in anyway.

### **3.9 DISSEMINATION OF RESULTS**

Findings from the study, was presented at the College of Health Sciences research seminar. A bounded copy of this research document was submitted to the Department of Chemical Pathology, University of Ghana Medical School in partial fulfilment for the award of a Master of Philosophy in Chemical Pathology Degree. Copies of this thesis dissertation were also submitted to the School of Graduate Studies and the Balme Library of the University of Ghana as reference material for further researches pertaining to physical exercise.

## CHAPTER FOUR

### 4.0 RESULTS

#### 4.1 Demographic and Characteristics of Study Subjects

The demographic and general characteristics of the study population are shown in Table 1. A total of 86 subjects comprising 44 (51.2%) females and 42 (48.8%) males took part in the study with an age range of 18-59 years. The subjects were made up of 42 cases (Gymnasium Attendees) comprising of 32 (76.2%) males and 10 (23.8%) females and 44 controls (apparently non-exercisers) consisting of 9 (20.5%) males and 35 (79.5%) females. There was no significant difference ( $p = 0.350$ ) between the mean age of the cases ( $29.1 \pm 9.6$ ) years and that of the controls ( $27.3 \pm 7.8$ ). Also, there was no significant difference in Systolic and Diastolic Blood Pressure, Physic Rating and Metabolic Age gave ( $p > 0.05$ ) between control and cases. However, there were significant differences ( $p < 0.001$ ) in height, weight, body mass index, heart rate, percentage body fat, muscle mass, visceral fat, daily calorie intake and bone mass between cases and controls (Table 1). Furthermore, significant difference ( $p = 0.03$ ) for visceral fat was obtained between cases (Table 1).

Table 1: Demographic Characteristics of Study Subjects

Characteristics	Controls	Gymnasium Participants	P-value
Age (yr)	27.3 ± 7.8	29.1 ± 9.6	0.350
Height (m)	1.6 ± 0.1	1.7 ± 0.1	<b>0.000*</b>
Weight (Kg)	67.3 ± 14.5	71.8 ± 14.3	<b>0.000*</b>
Body Mass Index (Kg/m <sup>2</sup> )	26.4 ± 4.3	24.7 ± 5.3	<b>0.014*</b>
Systolic Blood Pressure (mmHg)	112.8 ± 4.3	119.7 ± 12.0	0.160
Diastolic Blood Pressure (mmHg)	71.3 ± 8.7	76.7 ± 11.2	0.130
Heart Rate (bpm)	77.7 ± 12.2	90.4 ± 17.2	<b>0.000*</b>
Body fat (%)	27.1 ± 10.1	24.1 ± 9.4	<b>0.048*</b>
Total Body Water (%)	62.8 ± 7.6	53.2 ± 6.2	<b>0.041*</b>
Muscle Mass (Kg)	43.6 ± 7.1	55.1 ± 8.4	<b>0.000*</b>
Physic Rating	4.4 ± 1.5	3.7 ± 1.7	0.340
Daily Calorie Intake (Kcal/d)	2236.6 ± 494.0	3577.3 ± 628.7	<b>0.000*</b>
Metabolic Age (y)	27.2 ± 14.0	33.5 ± 13.1	0.320
Bone Mass (Kg)	2.3 ± 0.4	2.9 ± 0.5	<b>0.000*</b>
Visceral Fat	6.2 ± 4.6	3.5 ± 2.4	<b>0.030*</b>

*Table 1 shows comparison of the demographic and anthropometric characteristics between cases and controls. Data is presented as mean ± SD. \* p-value ≤ 0.05 is considered statistically significant.*

#### 4.2 Serum Biochemical Parameters of Subjects

Table 2 shows values for the serum biochemical analytes for both cases (Gymnasium attendants) and controls. Total cholesterol, triglyceride, HDL, and LDL showed statistical difference ( $p < 0.05$ ) between cases and controls. There was no significant difference between the case and control groups for VLDL-cholesterol and fasting blood glucose ( $p = 0.156$  and  $p = 0.648$ ) respectively.

Table 2: Serum Biochemical Parameters of Subjects

Parameters	Controls	Gymnasium Participants	P-value
<b>Total Cholesterol (mmol/L)</b>	5.28 ± 1.04	4.19 ± 1.60	<b>0.002*</b>
<b>Triglyceride (mmol/L)</b>	1.08 ± 0.43	0.94 ± 0.35	<b>0.014*</b>
<b>HDL-Chol (mmol/L)</b>	1.60 ± 0.51	2.04 ± 0.28	<b>0.000*</b>
<b>LDL-Chol (mmol/L)</b>	2.74 ± 0.90	2.27 ± 1.18	<b>0.002*</b>
<b>VLDL-Chol (mmol/L)</b>	0.49 ± 0.19	0.42 ± 0.16	0.156
<b>FBG (mmol/L)</b>	5.20 ± 1.80	4.98 ± 2.70	0.648

*Table 2 shows comparison of the biochemical parameters between cases and controls. Data is presented as mean ± SD. \* p-value ≤ 0.05 is considered statistically significant.*

### 4.3 Serum Antioxidant and Oxidative Stress Levels of Subjects

Results of measurements of antioxidants (SOD and UA) and oxidative stress (MDA) between the Gymnasium Attendants and controls are shown in Table 3. Gymnasium attendants had significantly higher uric acid, superoxide dismutase and malondialdehyde levels compared with controls ( $p < 0.05$ ).

Table 3: Serum Antioxidant and Oxidative Stress Levels of Subjects

Variables	Controls	Gymnasium Participants	P-value
Uric Acid ( $\mu\text{mol/L}$ )	293.672 $\pm$ 90.218	438.534 $\pm$ 142.702	<b>0.000*</b>
Superoxide Dismutase(U/L)	0.234 $\pm$ 0.042	1.525 $\pm$ 0.026	<b>0.000*</b>
Malondialdehyde ( $\mu\text{M}$ )	5.636 $\pm$ 2.267	8.948 $\pm$ 1.752	<b>0.000*</b>

*Table 3 shows comparison of the antioxidant and oxidative stress parameters between those who attend the gymnasium regularly (gymnasium participants) and controls. Data is presented as mean  $\pm$  SD. \*  $p$ -value  $\leq 0.05$  is considered statistically significant.*

#### 4.4 Correlation between Exercise, Antioxidants and Oxidative Stress in Gymnasium

##### Participants

Table 4 shows the association between antioxidants, oxidative stress and exercise intensity of study participants. Vigorous exercise correlated strongly with uric acid ( $r = 0.560$ ;  $p = 0.002$ ) and superoxide dismutase ( $r = 0.712$ ;  $p = 0.000$ ) but weakly with malondialdehyde ( $r = 0.431$ ;  $p = 0.006$ ). Although there was correlation between uric acid, malondialdehyde and moderate exercise, this was not statistically significant, however moderate exercise correlated strongly with superoxide dismutase ( $r = 0.817$ ;  $p = 0.000$ ). No significant association was found between walking, sitting and any of the antioxidants assessed.

Table 4: Correlation between Exercise, Antioxidants and Oxidative Stress Levels in Study Participants

EXERCISE INTENSITY		GYMNASIUM PARTICIPANTS		
		UA	SOD	MDA
<b>Vigorous</b>	r	<b>0.560</b>	<b>0.712</b>	<b>0.431</b>
	p	<b>0.002*</b>	<b>0.000*</b>	<b>0.006*</b>
<b>Moderate</b>	r	0.237	<b>0.817</b>	0.297
	p	0.820	<b>0.000*</b>	0.060
<b>Walking</b>	r	0.026	-0.188	-0.118
	p	0.873	0.240	0.469
<b>Sitting</b>	r	-0.160	-0.142	-0.142
	p	0.325	0.382	0.370

Table 4 shows the correlation between exercise, antioxidants and oxidative stress levels among the study population. Data is presented as mean  $\pm$  SD. \*P-value < 0.05 is considered statistically significant. Correlation coefficient  $r > 0.5$  represents strong positive correlation;  $r < 0.5$  shows weak positive correlation;  $r > -0.5$  shows strong negative correlation and  $r < -0.5$  shows weak negative correlation.

#### **4.5 Association between Antioxidant, Oxidative Stress and serum biochemical Parameters of Subjects**

The association between antioxidants, oxidative stress and serum biochemical parameters of subjects in this study is shown in Table 5. Among the control group, Uric acid showed a weak positive correlation with total cholesterol, triglyceride, HDL, LDL and VLDL respectively ( $r = 0.485$ ;  $p = 0.008$ ,  $r = 0.443$ ;  $p = 0.013$ ,  $r = 0.457$ ;  $p = 0.013$ ,  $r = 0.394$ ;  $p = 0.034$ ,  $r = 0.439$ ;  $p = 0.017$ ) respectively. For the case group, there was strong positive association between uric acid, superoxide dismutase, malondialdehyde and total cholesterol ( $r = 0.512$ ;  $p = 0.004$ ,  $r = 0.810$ ;  $p = 0.000$ ,  $r = 0.715$ ;  $p = 0.000$ ). SOD showed a weak positive correlation with FBG ( $r = 0.414$ ;  $p = 0.023$ ). Uric acid was found to be weakly but positively associated with HDL and LDL cholesterol ( $r = 0.455$ ;  $p = 0.012$  and  $r = 0.382$ ;  $p = 0.037$ ) with MDA strongly correlating positively with triglyceride ( $r = 0.841$ ;  $p = 0.000$ ) but weakly with LDL cholesterol ( $r = 0.403$ ;  $p = 0.023$ ) in gymnasium participants.

Table 5: Association between Antioxidant, Oxidative Stress and serum biochemical Parameters of Subjects

Parameters		Controls			Gymnasium Participants		
		UA	SOD	MDA	UA	SOD	MDA
<b>Total Cholesterol (mmol/L)</b>	r	<b>0.485</b>	-0.144	0.204	<b>0.512</b>	<b>0.810</b>	<b>0.715</b>
	p	<b>0.008*</b>	0.456	0.288	<b>0.004*</b>	<b>0.000*</b>	<b>0.000*</b>
<b>Triglycerides (mmol/L)</b>	r	<b>0.443</b>	0.005	-0.243	0.322	0.190	<b>0.841</b>
	p	<b>0.016*</b>	0.981	0.204	0.083	0.315	<b>0.000*</b>
<b>HDL (mmol/L)</b>	r	<b>0.457</b>	0.045	-0.129	<b>0.455</b>	0.058	0.179
	p	<b>0.013*</b>	0.818	0.505	<b>0.012*</b>	0.762	0.343
<b>LDL (mmol/L)</b>	r	<b>0.394</b>	-0.219	0.302	<b>0.382</b>	0.044	<b>0.403</b>
	p	<b>0.034*</b>	0.254	0.111	<b>0.037*</b>	0.818	<b>0.023*</b>
<b>VLDL (mmol/L)</b>	r	<b>0.439</b>	0.018	-0.289	0.295	0.195	0.078
	p	<b>0.017*</b>	0.925	0.128	0.113	0.302	0.684
<b>FBG (mmol/l)</b>	r	-0.187	0.066	-0.047	0.074	<b>0.414</b>	0.096
	p	0.331	0.732	0.808	0.699	<b>0.023*</b>	0.614

Table 5 shows the association between antioxidants, oxidative stress and serum biochemical parameters of study subjects. Data is presented as mean  $\pm$  SD. \*P-value < 0.05 is considered statistically significant. Correlation coefficient  $r > 0.5$  represents strong positive correlation;  $r < 0.5$  shows weak positive correlation;  $r > -0.5$  shows strong negative correlation and  $r < -0.5$  shows weak negative correlation.

#### 4.6 Association between Exercise Intensity and Lipid Profile in Gymnasium Participants

The association between exercise intensity and lipid profile in the gymnasium participants is shown in Table 6. Among the exercise group, vigorous intensity showed a weak positive correlation with total cholesterol, triglyceride and LDL respectively ( $r = 0.383$ ;  $p = 0.015$ ,  $r = 0.477$ ;  $p = 0.002$ ,  $r = 0.467$ ;  $p = 0.002$ ). Moderate intensity was found to be weakly but positively associated with triglyceride and LDL ( $r = 0.447$ ;  $p = 0.004$ ,  $r = 0.480$ ;  $p = 0.002$ ) respectively. However, walking and sitting intensity exercise showed no significant association ( $p > 0.05$ ) with lipid parameters (total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein) in the exercise group.

Table 6: Association between Exercise Intensity and Lipid Profile in Gymnasium Participants

EXERCISE INTENSITY		GYMNASIUM PARTICIPANTS				
		T. CHO	TRIG	HDL	LDL	VLDL
<b>Vigorous</b>	r	<b>0.383</b>	<b>0.477</b>	-0.001	<b>0.467</b>	0.307
	p	<b>0.015*</b>	<b>0.002*</b>	0.995	<b>0.002*</b>	0.054
<b>Moderate</b>	r	0.240	<b>0.447</b>	-0.197	<b>0.480</b>	0.212
	p	0.131	<b>0.004*</b>	0.216	<b>0.002*</b>	0.184
<b>Walking</b>	r	0.161	0.163	-0.043	0.106	0.170
	p	0.308	0.303	0.791	0.503	0.283
<b>Sitting</b>	r	-0.214	-0.012	-0.041	-0.148	-0.012
	p	0.186	0.941	0.802	0.361	0.942

Table 6 shows the association between exercise intensity and lipid profile in cases. Data is presented as mean  $\pm$  SD. \*P-value  $< 0.05$  is considered statistically significant. Correlation coefficient  $r > 0.5$  represents strong positive correlation;  $r < 0.5$  shows weak positive correlation;  $r > -0.5$  shows strong negative correlation and  $r < -0.5$  shows weak negative correlation.

#### 4.7 Association between Exercise Intensity and Lipid Profile in Controls

Table 7 shows the association between exercise intensity and lipid profile in the control group. Sitting intensity showed a weak negative correlation with total cholesterol and triglyceride ( $r = -0.345$ ;  $p = 0.027$ ,  $r = -0.338$ ;  $p = 0.031$ ) respectively. Vigorous exercise, moderate exercise, and walking showed no significant association ( $p > 0.05$ ) with lipid parameters (total cholesterol, triglycerides, high density lipoprotein, low density lipoprotein and very low density lipoprotein) in the control group.

Table 7: Association between Exercise Intensity and Lipid Profile in controls

EXERCISE INTENSITY		CONTROLS				
		T. CHO	TRIG	HDL	LDL	VLDL
<b>Vigorous</b>	r	0.151	0.186	0.299	0.170	0.174
	p	0.434	0.335	0.115	0.379	0.367
<b>Moderate</b>	r	-0.060	0.228	0.189	-0.009	0.199
	p	0.756	0.233	0.325	0.965	0.301
<b>Walking</b>	r	0.065	-0.194	-0.261	0.190	-0.168
	p	0.742	0.324	0.181	0.333	0.303
<b>Sitting</b>	r	<b>-0.345</b>	<b>-0.338</b>	-0.292	-0.248	-0.041
	p	<b>0.027*</b>	<b>0.031*</b>	0.139	0.213	0.839

Table 7 shows the association between exercise intensity and lipid profile in controls. Data is presented as mean  $\pm$  SD. \*P-value  $< 0.05$  is considered statistically significant. Correlation coefficient  $r > 0.5$  represents strong positive correlation;  $r < 0.5$  shows weak positive correlation;  $r > -0.5$  shows strong negative correlation and  $r < -0.5$  shows weak negative correlation.

## CHAPTER FIVE

### 5.0 DISCUSSION

The aim of the study was to investigate the effect of regular exercise on circulating antioxidant defences and selected biochemical health indicators in Ghanaian individuals using malondialdehyde (MDA), superoxide dismutase (SOD) and uric acids (UA) as oxidative stress markers and antioxidant biomarkers during resting conditions in exercise participants and comparing them to sedentary controls. Biochemical parameters such as fasting blood glucose, lipid profile (LDL-C, HDL-C, total-cholesterol and triglycerides) as well as anthropometric characteristics, metabolic age, height, weight, body mass index, systolic and diastolic blood pressure, heart rate, total body fat and water, muscle and bone mass, physic rating, daily calorie intake and visceral fat were also determined.

Body mass index (BMI) classification by WHO, (2003) outlines 18.5-24.9 as normal weight, 25-29.9 as overweight and equal to or greater than 30 kg/m<sup>2</sup> as obese. The significantly higher body weight in gymnasium participants (Table 1) is as a result of increased participation in vigorous and moderate intensity exercises (Table 4), increased energy expenditure which is reflected in their increased daily calorie intake and increased muscle mass (Table 1). Caloric intake is positively associated with exercise (Calbet *et al.*, 2015) and caloric expenditure is higher in the exercise groups and is in agreement with an earlier study (Falcone *et al.*, 2015). This is evident in the significantly high levels of daily calorie intake, muscle and bone mass as well as visceral fats observed in the gymnasium participants. It has been reported that BMI may correlate with oxidative stress and MDA levels (Furukawa *et al.*, 2004). Superoxide dismutase in obese people was lower when compared with slim people (Fernández-Sánchez *et al.*, 2011; Palacios *et al.*, 2015). The strong positive correlation of vigorous exercise with SOD in the exercise group (Table 5) may suggest the possible direct response of SOD as an endogenous enzyme to decrease

lipid peroxidation during exercise. Superoxide dismutase acts as a detoxification enzyme as it converts the oxygen radicals produced during intense exercise (Giimiistas, 2003) to hydrogen peroxide.

In this study, the effects of exercise on lipid peroxidation showed significant difference between control and exercise groups (Table 3). The findings were in agreement with Maughan *et al.*, (1989); Çakir-Atabek *et al.*, (2010); Kiyici and Kishali, (2012) and Olcucu (2015) but were not in agreement with the findings of Vasankari *et al.*, (1995); Dixon *et al.*, (2006) and Elabed *et al.*, (2015). Differences in race, environment, physiological nature, intensity and frequency of exercise performed as well as the decrease in levels of MDA during rest levels after exercising all contributed to differences in this study. Changes in lipid metabolism during exercise may have some effect on the MDA levels. It has been shown that exercise enhances the body's ability to utilise the lipids in the body (Earnest *et al.*, 2013). A possible explanation is the mechanism of transfer of an ester group to HDL-C following increase levels of lecithin-cholesterol acyltransferase (LCAT) increasing the HDL-C during exercise (Calabresi and Franceshini, 2010; Riedle *et al.*, 2010).

Levels of uric acid (UA) in the exercise group (Table 3) were highly elevated and significant ( $p < 0.05$ ). Uric acid as an antioxidant, prevents damage by lipid peroxidation (Ames *et al.*, 1993) scavenge peroxy radicals (Muraoka and Miura, 2003) and may react with oxygen from free radicals during high intensity exercise (Hellsten *et al.*, 1997). Studies by Aruoma *et al.*, (1989); Mikami *et al.*, (2000); Waring *et al.*, (2003) and Huang *et al.*, (2010) have found increased levels of UA in exercise groups after resting conditions. Increases in uric acid may be attributed to the high calories being used by the body for energy during exercise. It may also be related to the build-up of lactic acid generated due to

the high intensity exercise that competes with uric acid for excretion (Table 4). Thus elevated levels may be attributed to intense training, energy demand and less muscle damage as well as dehydration (Palacios *et al.*, 2015). Further to that, increased uric acid levels may prevent lipid peroxidation after exercise (Ames *et al.*, 1993; Muraoka and Miura, 2003) possibly contributing to the decrease in MDA levels in the exercise group. Uric acid levels correlated with changes in biochemical parameters such as lipid profile (Table 5). Change in LDL susceptibility due to oxidation during exercise may lead to the production of uric acid during intense exercise (Benitez *et al.*, 2002).

Biochemical parameters such as fasting blood glucose, high density lipoprotein cholesterol (HDL-C) and very low density lipoproteins cholesterol (VLDL-C) showed no significant association with MDA and SOD in the two groups (Table 5). However, total cholesterol, triglycerides, LDL-C and HDL-C showed significant difference between the two groups (Table 2). Singh and Sankhla, (2015) found aerobic exercise to have positive effect on lipid levels and suggested that the inclusion of aerobic exercise in lifestyle practices will reduce the risk factors associated with diabetes and cardiovascular disease. The findings (total cholesterol, triglycerides, LDL-C and HDL-C) observed between the two groups in this study supports previous investigation (Harris, 1999). When Hinkleman and Neiman (1993) compared exercise and non-exercise groups, they observed an increase in HDL-C levels in non-exercise groups and a reduction in exercise group. Conversely, Smoak *et al.*, (1990) found no change in lipid profile after intense physical conditioning. The significant high levels in HDL-C in the exercise group in this study, agrees with the findings of Escalante *et al.*, (2012) who examined the different volumes and intensities of exercise on the different cholesterol levels and found that combined exercise improves the HDL-C. An increase in HDL-C may suggest a healthy cardiovascular system (Carroll *et al.*, 2012) though the gold standard in preventing cardiovascular risk is reduced total cholesterol levels (Whayne,

2011). The exercise group demonstrated reduced level of total cholesterol as compared to controls (Table 2 and Table 6) in this study.

A meta-analysis to examine the effect of walking on lipids and lipoproteins in adults found a reduction in LDL-C but showed no statistical difference in total cholesterol, triglyceride and HDL (Kelley *et al.*, 2004). Leon *et al.*, (1979) in their study found that vigorous walking by obese young adults increased HDL by 15.6% but triglyceride and total cholesterol showed no changes. In this study regular walking (at work, home to travel, from place to place, for recreation, sport, exercise or leisure) did not affect levels of lipids in both groups (Table 6 and Table 7) but sitting intensity-time spent sitting on weekdays at work, at home, while doing course work and during leisure time as well as time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television in the controls could cause increased total cholesterol and triglyceride (Table 7). Triglyceride is independently associated with cardiovascular disease (Luz *et al.*, 2008) and it is obtained from fats eaten in food or other energy sources. A recent meta-analysis have shown that people who sit too much every day may be at an increased risk of diabetes, heart disease, cancer and short life span even if they exercise (Biswas *et al.*, 2015).

## **6.0 CONCLUSION**

Results from this study showed significant higher levels of weight, height, heart rate, visceral fat, daily calorie intake, muscle and bone mass in people who exercised both vigorously and moderately as compared to sedentary controls. The study revealed significantly higher uric acid levels in gymnasium participants than in controls. Furthermore, the exercise group that participated in vigorous and moderate exercise intensities had higher HDL-C than the control group. Oxidative stress MDA and antioxidant SOD markers were significantly higher ( $p < 0.05$ ) in the exercise group compared to controls. Regular exercise may have beneficial impact on antioxidants and some biochemical health parameters in exercise subjects. However there is no doubt that regular exercise has some benefits on both antioxidants and biochemical factors in health.

## **6.1 LIMITATIONS**

This research had several limitations. Financial constraint was a major challenge limiting analysis of only a few antioxidant, oxidative stress and biochemical markers. Unwillingness from participants and managers of gymnasium centres to grant permission, and time constraints, restricted the selection of subjects across the many gymnasium centres. It is therefore recommended for a similar study to be carried out in the various exercise categories in the gymnasium centres.

## 6.2 RECOMMENDATION

- A longitudinal study on the duration, intensity and frequency of exercise individuals of people who regularly visit the gymnasium centres should be carried out, taking into account their dietary patterns.
- Genetic studies in the areas of Apo proteins in exercise groups in the gymnasium should be conducted as these may influence the levels of lipids
- A more specific definition for the various exercise groups such as those that use the treadmill, do push ups, weight lift and indulge in any form of exercise when they visit the gymnasium centres should be used to ascertain what the situation is like in Ghana.
- Findings from this study in addition, suggest the need for pragmatic steps in reducing the incidence of non-communicable diseases.
- Responses of lipid profile to exercise training are dependent on the type of exercise, intensity, frequency as well as the duration and time (Cox *et al.*, 2001). As this research did not take into account differences in dietary patterns and individual types of exercise performed in the gymnasium, a long term research in inter-exercise groups should be carried out.

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**APPENDIX I**  
**INFORMED CONSENT FORM**

I, **Patrick Diaba-Nuhoho** of the Department of Chemical Pathology, University of Ghana Medical School (UGMS) wish to embark on a research study titled **The Impact of Regular Exercise on Antioxidant and Selected Biochemical Health Indicators**.

The purpose of this study is to investigate the effect of regular exercise on circulating antioxidant defences and selected biochemical health indicators.

I will ask you few routine questions about your personal details, exercise history etc. The benefits of the study are to educate you on exercise, its benefits and dangers. Also to ascertain the health burden of Non-Communicable Disease (NCDs) on the nation in terms of cost and mortality. I humbly implore you to volunteer, though participation is entirely voluntary and strictly confidential. You may choose to withdraw from the study whenever you wish. You will be required to have an overnight fast. The amount of blood to be taken by phlebotomists and used for this research study will not exceed 10mls (less than three tea spoonful).

You will be assured of the strictest confidentiality of your personal information. This study will adhere to all applicable protocol and maintain quality assurance in accordance with good laboratory practice. The blood samples collected will bear an identification code to ensure anonymity, confidentiality and ease of identification. There is a possibility you might not benefit directly from participation. In addition, the information obtained and conclusions drawn will be applied in the adoption of relevant health policies as well as the appropriate care and management. You will incur no costs and you will also not be paid for participating in this research. All data will be entered onto a lock/word-protected Microsoft Excel spreadsheet. Study questionnaires will be kept in a locked cabinet in a locked office. My contact numbers are **0243558331/0286558331**. You may call me for any further clarification.

Thank you for the cooperation and anticipated compliance to the study requirements.

Signature: ..... Date: .....

**APPENDIX II**  
**PARTICIPANT CONSENT RESPONSE**

**Research title:     The Impact of Regular Exercise on Antioxidant and Selected Biochemical Health Indicators.**

I, ..... have been invited to take part in this research. I have been told of the purpose and procedure of this study which is to answer the questions raised about the effect of regular exercise on circulating antioxidant defences and selected biochemical health indicators such as lipids, fasting blood sugar and uric acid. I will be asked a few routine questions about personal information such as my educational background, exercise history etc. I will not be reimbursed monetarily for participating in this research study.

The risk or dangers and discomforts might involve the pain of blood collection. The study team will try to reduce the chances of those risks happening by employing trained phlebotomist. The arm will be sanitized before blood collection, and new sterile needles and gloves will be used for each participant. I promise to comply with this research study and I consent accordingly.

Signature.....

Thumbprint.....



18. Occupation       Unemployed  
                          Trader/Self employed  
                          Government worker  
                          Others (pls. specify):.....

19. Ethnicity         Akan  
                          Ga  
                          Ewe  
                          Northerner  
                          Others (pls. specify):.....

**MEDICAL HISTORY**

1. Do you have any of the following conditions?  
                          Chronic Kidney Disease  
                          Hypertension  
                          Diabetes Mellitus  
                          Others (please specify  
                          None

**HERBAL REMEDIES AND OTHER HEALTH PRODUCTS**

1. Are you taking any herbal remedy or preparation?       Yes                       No  
2. Are you taking any vitamins or antioxidant therapy?     Yes                       No

## INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

I am interested in finding out about the kinds of physical activities that you do as part of your everyday life. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

\_\_\_\_\_ **days per week**

No vigorous physical activities → *Skip to question 3*

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

\_\_\_\_\_ **hours per day**

\_\_\_\_\_ **minutes per day**

Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

\_\_\_\_\_ **days per week**

No moderate physical activities → *Skip to question 5*

4. How much time did you usually spend doing **moderate** physical activities on one of those days?

\_\_\_\_\_ **hours per day**

\_\_\_\_\_ **minutes per day**

Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you have done solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

\_\_\_\_\_ **days per week**

No walking → *Skip to question 7*

6. How much time did you usually spend **walking** on one of those days?

\_\_\_\_\_ **hours per day**

\_\_\_\_\_ **minutes per day**

Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**.

Include time spent at work, at home, while doing course work and during leisure time.

This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

\_\_\_\_\_ **hours per day**

\_\_\_\_\_ **minutes per day**

Don't know/Not sure

**This is the end of the questionnaire, thank you for participating.**

APPENDIX IV

SCHOOL OF MEDICINE AND DENTISTRY  
COLLEGE OF HEALTH SCIENCES  
UNIVERSITY OF GHANA  
ACADEMIC AFFAIRS OFFICE

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My Ref. No: MS-AA/C.2/Vol.18<sup>A</sup>



P O Box 4236  
Accra  
Ghana

7<sup>th</sup> January, 2015

Your Ref. No.

**Mr. Patrick Diaba-Nuhono**  
Department of Chemical Pathology  
SBAHS  
Korle-Bu

**ETHICAL CLEARANCE**

Protocol Identification Number: **MS-Et/M.4 – P 4.2/2014-2015**

The Ethical and Protocol Review Committee of the School of Medicine and Dentistry on 7<sup>th</sup> January, 2015 unanimously approved your research proposal.

**TITLE OF PROTOCOL: "The Impact of Regular Exercise on Antioxidants and Selected Biochemical Health Indicators"**

**PRINCIPAL INVESTIGATOR: Mr. Patrick Diaba-Nuhono**

This approval requires that you submit six-monthly review reports of the protocol to the Committee and a final full review to the Ethical and Protocol Review Committee at the completion of the study. The Committee may observe, or cause to be observed, procedures and records of the study during and after implementation.

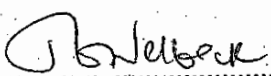
Please note that any significant modification of this project must be submitted to the Committee for review and approval before its implementation.

You are required to report all serious adverse events related to this study to the Ethical and Protocol Review Committee within seven (7) days verbally and fourteen (14) days in writing.

As part of the review process, it is the Committee's duty to review the ethical aspects of any manuscript that may be produced from this study. You will therefore be required to furnish the Committee with any manuscript for publication.

**This ethical clearance is valid till June, 2016.**

Please always quote the protocol identification number in all future correspondence in relation to this protocol.

Signed:   
.....

PROFESSOR JENNIFER WELBECK  
CHAIRPERSON, ETHICAL AND PROTOCOL REVIEW COMMITTEE

cc: Dean, SMD  
Head of Department  
Research Office

**APPENDIX V****BUDGET AND LOGISTICS**

Item	Quantity	Unit cost (GH¢)	Total cost (GH¢)
Stationary and writing materials	5 rims	13.80	69.00
Printing of proposal	12 copies of 25pp	0.23	69.00
Thesis and Binding	5 copies of 350pp	0.23	402.50
Cotton	1 roll	18.40	18.40
Gloves, Tourniquets	4 boxes, 2 sets	43.00	132.00
Phlebotomist plaster	2 boxes	28.75	57.50
Methylated spirit	1 litre	17.25	17.25
Eppendorf tubes	1 pack	46.00	46.00
Pipette tips	200	43.70	43.70
Syringe/Needles	2 boxes	20.00	40.00
Serum separator tubes	2 packs	57.50	115.00
Fluoride oxalate tubes	2 packs	46.00	92.00
Glucose Oxidase reagent	2 boxes	300.00	600.00
Triglyceride reagent	2 boxes	172.50	345.00
Total Cholesterol reagent	2 boxes	250.00	500.00
HDL reagent	2 boxes	103.50	207.00
Uric acid reagent	2 boxes	124.00	248.00
Superoxide Dismutase(BioAssay, USA)	2 boxes	920.00	1840.00
Malondialdehyde ELISA Kit(BioAssay, USA)	2 boxes	510.00	1020.00
Shipping and Clearing			1320.00
<b>Grand Total</b>			<b>7182.35</b>