EFFECT OF AEROBIC TRAINING ON SERUM GLUCOSE, INSULIN, GLUCAGON, LIPIDS AND LIPOPROTEINS OF OVERWEIGHT NIGERIAN MALE ADULTS

BY

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BY

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JUNE, 2015

DECLARATION

I hereby declare that this dissertation has been written by me and that it is a record of my own research work. It has not been presented in a previous application for higher degree. All quotations have been indicated and the sources of information were specifically acknowledged by means of reference.

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Michael Habu Shuaibu DUWAI Date

CERTIFICATION

This dissertation entitled: "**Effect of Aerobic Training on Serum Glucose, Insulin, Glucagon, Lipids and Lipoproteins of Overweight Healthy Nigeria Male Adults"** by **Michael Habu Shuaibu DUWAI,** meets the regulations governing the award of the degree of Doctor of Philosophy in Exercise and Sports Science, Ahmadu Bello University, Zaria, and is approved for its contribution to knowledge and literary presentation.

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ABSTRACT

The study investigated the effect of aerobic training on serum glucose, insulin, glucagon, lipid and lipoproteins of overweight Nigerian male adults. The aerobic training program comprised of walking and jogging with stretching activities at the beginning and at the end of each training session. Seventeen (17) overweight male adults between the ages of 25 and 35 years volunteered to participate in this study. For the purpose of this study, an experimental study using one group repeated trials research design in which subjects were given different treatments at different times, was used. In this design, subjects underwent moderate intensity walk-jog aerobic training on three (3) alternate days per week between 40 and 45% HR max for 30 minutes within the first three 3 weeks; 45% and 50% HR max for 35 minutes from week 4 to 6; 50 and 55% HR max for 40 minutes from week 7 to 9, and 55 and 60 % HR max for 50 minutes from week 10 to 12. RPE scale was used to monitor the exertion of training throughout the research period. All subjects were tested for fasting blood glucose, insulin, glucagon, lipids and lipoproteins before starting the training (baseline), was repeated after 6^{th} and 12^{th} week of training. Blood samples for the determination of these variables were assayed at the Chemical Pathology Laboratory, Ahmadu Bello University Teaching Hospital, Zaria. The data collected were statistically analysed using descriptive and repeated measures analysis of variance (ANOVA). The results of the study revealed significant decrease n serum insulin, triglycerides and total cholesterol and significant increase in serum glucagon due to 12 weeks of moderate aerobic training.. The study did not reveal significant decrease in serum glucose, low density lipoproteins and significant increase in high density lipoproteins due to 12 weeks moderate intensity aerobic training. It was concluded that moderate intensity aerobic training conducted at 40-60% HR max for between 30 and 50 minutes on 3 alternate days a week had significant effect on serum insulin, triglycerides and total cholesterol and significant increase in serum glucagon of overweight Nigerian male adults. Since walking/jogging was found to significantly improve hormonal regulatory role of insulin and glucagon on glucose utilization, it was suggested that health professionals and fitness centres should use this method of training on overweight adults reduce insulin resistance, impaired glucose transport and improve insulin sensitivity.

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1.9 Operational Definition of Terms

Moderate intensity. An aerobic training programme with the intensity between 40 and 60% HR max

Aerobic training. Jogging - walking training programme of low intensity that lasted between 30 and 50 minutes.

Rating of Perceived Exertion. A scale rating of exercise exertion used to estimate the intensity of tainting for which the participant did not need to stop in order to check his heart rate.

CHAPTER ONE

INTRODUCTION

1.1 Background of the study

Being overweight is associated with many medical problems, such as hypertension, diabetes, and heart diseases. Overweight people are more likely to lead sedentary lifestyle, and if they decide to start exercise program, are usualy successful. By age 30, both average male and female fall in the overweight category, and by age 50 years, they fall in the obesity category (Strand & Wallace, 2005; Plowman & Smith, 2008).

Physical inactivity, increase in body weight and fat percent, are associated with higher incidence of impaired glucose tolerance, insulin resistance and type 2 diabetes mellitus (T2DM). People who are overweight and obese are more prone to heart disease, certain form of cancer (Lakka& Laaksonen, 2007; Colberg & Greico, 2009). This is potentially contributing to the development of cardiovascular diseases and micro vascular complications, like neuropathy and blindness (Muller, Elahi, Tobin, & Andros, 1996; Neel, Weder & Julius 1998; Coker, Hays, Williams, Brown, Freeling, Korterbein & Evans, 2006; Venkateswarlu, 2010; khorshidi, Assarzadeh, Beni, Abedi & Ezadi, 2012). In the case of diabetes, the risk increases approximately 10 fold once a BMI of 30kg/m^2 is reached, and the more obese, the greater the relative risk (Lindholm, Agardb & Tuomi, 2002).

T2DM is preceded by a cascade of events that take several years to develop, including insulin resistance, followed by glucose intolerance and hyperinsulinemia, which may result in insulin deficiency (Ostrow & Dzewltwski, 1986; Mayfield, 1998; Galloway & Jokl, 2000; Choi, Lee & Youn,; 2001). The physiological progression of insulin resistance in type 2 diabetic patients results in a variety of health related complications, like visual loss, loss of functional

independence and a higher rate of mortality (Reavens, 1995; King, Albert & Herman, 1998; Ford, 2005; American College of Sport Medicine, Chodzleo-Zoyko, Proctor, Flatarone-Singh, Minson, Nigy, Salem & Sknner, 2009).Therefore, the medical, psychological and financial burdens of this adverse squealae necessitates the determination of appropriate interventions to promote insulin sensitivity and reduce the risk of type 2 diabetes mellitus (T2DM) among overweight adults in Nigeria.

Many components of metabolic syndrome are associated with overweight and sedentary lifestyle, including increased adipose tissue, cholesterol, triglycerides, blood glucose, low density lipoprotein, blood pressure and reduced high density lipoprotein (American Diabetes Association, 2003; Hu, 2003; Huang, Ball & Frauls, 2007; Habibzadeh, 2010).

Overweight people are more likely to possess high blood sugar, and are known to be diabetic. It is essential to normal health that the serum glucose be maintained around 80 and 90 mg per 100cc of blood in well nourished individual (Irwin, Mayer-Davis, & Addy, 2000; Ruderman, Devlin, Schneider & Kriska 2001 Khaw, Wareham, Bingham, Luben, Walch & Day, 2004; American Diabetic Association, 2008). Diabetes being one of the major chronic metabolic disorders associated with overweight is a disorder of glucose metabolism (Tauton & McCargarl, 1995; King & Hermann, 1998; Williams, 2007, Plowman & Smith, 2008) and characterized by hyperglycemia.

Insulin and glucagon are responsible for glucose homeostasis, minute- to-minute regulation of the body's integrated metabolism and stabilizing the body's milieu or interior (Voet & Voet, 1995; Kang, Robertson, Hagbert, Keleey, Goss, Dastlva, Suminski & Utter 1996; Libman & Arslanian, 1997; Ganong, 2001; 2011). Insulin resistance is a physiological abnormality that increases the likelihood that one or more of the abnormalities will be present in overweight individuals (Yu, Chen, & Cline, 1991; Paollisso & Howard, 1998; Reavens, 2005).

Increased lipids availability may increase the activity of the hexosamine pathway, a quantitatively small route of glucose metabolism that functions as a nutrient sensing mechanism, but has been implicated in the development of insulin resistance (Rossetti, 2000; Assail, Ganor, Shafer & Hershcoici, 2001). Aberrant lipid metabolism, particularly increased lipids availability is implicated in the cause of metabolic syndromes in overweight persons (Philips, Caddy,& Illic, 1996). Hyperlipidemia and hyperlipoproteinemia, such as increased triglycerides and total cholesterol, decreased high density lipoproteins and increased low density lipoproteins, have been reported to be associated with individuals whose BMI exceeds 25kg/m2 (Romijn, Coyle, Sidoscis, Gasteldelli, Horowitz Endert & Wolfe, 1993).Triglycerides (TG) are other fats in body serum. Many people who have heart disease or diabetes have high TG level. Cholesterol (TC) also plays a major role in human heart health. High cholesterol in serum is a leading risk factor for human cardiovascular disease (Exercutiv Summary of the Third Report of the NCEP, 2001; Wildman & Miller, 2004; Williams, 2007).

High density lipoproteins (HDL) is a protein complex in the blood that facilitates the transport of 45-50% of moderate amount of cholesterol, phospholipids and little TG, and a medium through which cholesterol is transported in blood . HDL levels are protective against coronary heart disease (CHD) and diabetes (Broun & Cargill, 2002; Farhan & Michael, 2008). Low density lipoproteins facilitate the transport of TG, TC and phospholipids (Broun & Cargill, 2002; Vantone, 2002). Studies have shown that overweight and obesity are associated with sedentary lifestyle, reduced HDL-C and increased LDL-C (Hegarty, Furler, Ye, Cooney & Kraegen 2003; Williams, 2007; khorshidi et al; 2012).

Studies have shown that exercise training reduces abnormal levels of serum glucose and impaired glucose transport, reduces insulin resistance and enhances insulin and glucagon regulation of glucose, reduces lipids concentration, and tends to increase HDL-C and decrease LDL-C (Coggan, Swanson, Mendenhal, Habash Kien, 1995; Pierce, 1999; Bergman, Horning,

Casazza, Wolf, Butterfied & Brooks, 2000; Coker & Kjaer, 2005; Sigal, Kenny, Wasserman, Castandeda-Scoppa & White, 2006, Van der Heijden, Toffolo, Manesse, Saur, Surehag, 2009; Holloszy, 2013; Krishna, Coker, Lacy Zinker, Halsetti, Wasseyman. 20013). The Consumers Union (2005), report on the use of alternative treatment for various health problems, noted that aerobic exercise is one of the most effective methods. In support of this viewpoint, Plowman & Smith, (2008), indicated that regular physical activity reduces peopple's risk of heart attack, certain cancer, type 2 diabetes and high blood pressure. The combinations of exercise and weight loss have been shown to produce numerous health benefits, including decreased blood pressure, improved serum lipid status, reduced blood glucose and improved psychological health (Wildman & Miller, 2004; Williams, 2007). Ciccine, (2001), Wildman & Miller, (2004), Williams, (2007), stressed that to achieve greater physiological effects, exercise should primarily be aerobic because it offers more oxygen to the working muscles.

Considering the improvement of insulin sensitivity and glucose transport, the role of glucagon in the regulation of blood glucose, and the reduction of lipids and improvement in lipoproteins levels during in fit individuals, it is essential to find out the effects of aerobic training on serum glucose, insulin, glucagon, lipids and lipoproteins of overweight Nigerian male adults, results of which will be helpful in the control and management of overweight and obesity.

1.2 Statement of the Problem

The prevalence of overweight in adults is a cause for concern as overweight is associated with a wide variety of conditions and metabolic abnormalities, including diabetes and elevated blood pressure (Al-sendi, Shetty, Musaiger & Myatt, 2003). The problem and health risk associated with adults that are overweight are often played down, although, overweight and obesity are leading risk for global deaths. Alarmingly, overweight (BMI < 30) have 50-100% increase risk of premature deaths compared with healthy weight (Wildman & Miller, 2004;

Williams, 2007). Around 3.4 million adults die each year as a result of being overweight or obese. In addition, 44% of the diabetes burden, 23% of the ischemic heart disease burden and between 7% and 41% of certain cancer burdens are attributed to overweight and obesity (Magashi, 2014).

Overweight and obesity are considered a single disease entity that constitutes most serious health problems in the world today (Strand & Mallace, 2005; Plowman & Smith, 2008). People who are overweight or obese possess excess blood sugar, insulin resistance, high triglycerides and cholesterol, low high density lipoproteins and high low density lipoproteins (Goodman & Whitaker, 2002; Makinde, 2012). This represents a significant health risk in overweight persons (Plowman & Smith, 2008). Worldwide, about 80% of diabetes mellitus and 21% of ischaemic heart diseases are attributed to body mass index (BMI) above 21kg/m^2. BMI is positively and independently associated with mortality from hypertension, cardiovascular diseases, T2DM, and other chronic diseases.

Although, studies have documented an increase in the prevalence of health risks in overweight and obese middle age male adults (Al-Mousa &Parkash, 2000; Musaiger, Al-Ansari & Al-Monrai, 2000), however, little has been done by exercise scientists to investigate the effect of aerobic training (walking/jogging) on serum glucose, metabolic hormones (insulin and glucagon), lipids and lipoproteins of overweight Nigerian male adults. Patients with impaired glucose tolerance in type 2 diabetes have been shown to be overweight and characterized by having sedentary lifestyle coupled with low physical fitness level and insulin resistance (Evans, Van, Pelt, binder, Williams, Ehsan, & Kohrt, 2001; Sato, Nagasaki, Nakai, & Fushimi, 2003).

The value of exercise training for overweight individuals goes beyond the sometimes minor contribution to weight loss (Powers and Howley, 2012). Continued physical training has been shown to improve reduced peripheral tissue sensitivity to insulin in impaired glucose tolerance and type 2 diabetes (Borghouts & Keizer, 2000; Kelley & Good, 2011), and also to

improve abnormal lipid metabolism. Changes in insulin and glucagon due to training appear to play a significant role in glucose homeostasis (Wolfe, Nedel, Shaw, Stephenson & Wolfe 1986). It is not clear whether moderate intensity aerobic training (30-60% of $Vo_{2\ max}$ or <40- 60% maximal heart rate) through rating perceived exertion [RPE]) would cause favourable changes in serum insulin, glucagon, lipids and lipoproteins of overweight male adults. T2DM being one of the major chronic metabolic disorders precipitated by hyperglycemia and associated with higher incidence of insulin resistance, hyperlipidemia and sedentary lifestyle (Irwin et al; 2000; Hegarty et al; 2003; Ochei Okolhalkar, 2007; Williams, 2007; Plowman & Smith, 2008), is considered a more health concern that affects overweight adults. An improvement in the abnormal concentration of these variables through walking/jogging would make aerobic training a preventive measure of T2DM.

Abnormal or high serum glucose/impaired glucose transport, hyperinsulinemia or insulin deficiency, and aberrant lipids metabolism, particularly increased lipids availability, constitute serious health risk that may result in metabolic syndrome in overweight persons (Lamonte et al; 2005; Dullo, 2005; Boushed, Gnaiger, Schjerling, Skovbro, Kraunsoc & Dela, 2007, Shaibi, Robert, & Goran 2008). As sedentary lifestyle is attributed to the abnormal concentration of these variables in overweight individual, exercise training may be beneficial in the management of these abnormalities (Roy Parker, 2007; Plowman Smith, 2008; Powers Howley, 2012). Considering the health implications associatd with abnormal serum glucose, insulin resistance, aberrant lipids and lipproteins in overweight persons, this warrants the investigation of the effect of aerobic training on serum glucose, insulin, lipids and lipoproteins of overweight Nigerian male adults.

1.3 Research Questions

This investigation was to answer the following specific research questions.

1. Would walk/jog program modify serum glucose concentration of overweight Nigerian male adults?
2. Would aerobic training modify serum insulin concentration of overweight Nigerian male adults?
3. Would aerobic training modify serum glucagon concentration of overweight Nigerian male adults?
4. Would aerobic training modify serum lipids concentration of overweight Nigerian male adults?
5. Would aerobic training modify serum lipoproteins of overweight Nigerian male adults?

1.4 Basic Assumptions

The following assumptions were made for the purpose of the study:

1. Physical training at moderate intensity reduces the risk factors of metabolic syndrome.
2. The effect of aerobic training on serum glucose depends on the intensity of training and also on the training condition and glucose level of the individual.
3. The effect of physical training on disease risk factors depends on the initial level of these factors.
4. The effect of aerobic training on insulin and glucagon dependends on the intensity of the activity and the level of glucose deplection.
5. The effect of aerobic exercise training on lipids and lipoproteins depends on the intensity and duration of training.

1.5 Hypotheses

On the basis of the research questions, the following hypotheses were formulated for the purpose of the study.

1.5.1 Major Hypothesis

There are no significant effects of aerobic training on serum glucose, insulin, glucagon, lipids and lipoproteins of overweight Nigerian male adults.

1.5.2 Sub-Hypotheses

1. There is no significant effect of aerobic training on serum glucose levels of overweight Nigerian male adults.
2, There is no significant effect of aerobic training on serum insulin levels of overweight Nigerian male adults..
3. There is no significant effect of aerobic training on glucagon levels of overweight Nigerian male adults.
4. There is no significant effect of aerobic training on lipids levels of overweight Nigerian male adults.
5. There is no significant effect of aerobic training on serum lipoprotein of overweight Nigerian male adults..

1.6 Significance of the Study

The study was justified on the following bases.

As this study was conducted on overweight individuals who underwent training for 12 weeks, the results of the study will show whether the effects of aerobic training on serum glucose level of overweight individuals will be similar to those observed in diabetics. Such information would assist the overweight adult to maintain a euglycemic state through aerobic training.

This study involved the assay of insulin among overweight Nigerian male adults who participated in 12 weeks aerobic training, it would show whether aerobic training had any positive effect on insulin. This information will be useful in recommending exercise training fot the reduction of insulin resistance and to promote insulin sensitivity in overweight adults.

The effects of glucagon on blood glucose level are reciprocal to those of insulin. It is not clear whether exercise training brings about significant effects on both insulin and glucagon at the same time or at different times depending on blood glucose levels of overweight individuals. Results of the study would show the counter regulatory effects of aerobic training on glucagon. Such results will be helpful in prescribing exercise to improve the activities of insulin and glucagon in maintaining glucose homeostasis in overweight adults.

The results of previous studies on the effects of aerobic exercise training on serum lipids and lipoproteins are inconsistent. The results of this study would show the effect of aerobic training (walking/jogging) on lipids and lipoproteins, as high intensity exercise training has been reported to be more effective in lipids and lipoproteins regulation. Such information will be helpful in prescribing exercise programs for overweight adults who would want to improve their TG, TC HDL-C and LDL-C levels.

This study might bring to light new areas related to training intensity on glucose, metabolic hormones, lipids and lipoproteins as the training used in this study was moderate intensity aerobic training (walking/jogging) for further research.

1.7 Delimitations of the Study

The study was delimited to the following :

1. The 12 weeks walking/jogging was to evaluate the effect of aerobic training on serum glucose, insulin, glucagon, lipids of overweight Nigerian male adults.

2. The lipids investigated in this study were triglycerides and total cholesterol, whereas, the lipoproteins investigated included high density lipoproteins and low density lipoproteins.

3. The training intensity given was from < 40-60% (very light – moderate) heart rate max [HR max] for 30 or more minutes, which was followed on 3 alternate days a week for 12 weeks.

4. The subjects for this study were overweight male students from ECWA College of Health Technology, Kagoro, Kaduna State, between the ages of 25-35 years.

1.8 Limitations of the study

This study had the following limitations which were taken into consideration while interpreting the results.

1. Studies have shown that physical training conducted at high intensity produced better physiological results in serum glucose, lipids, lipoproteins and hormones. As this study was conducted on overweight male adults without any structured physical training background, the intensity of training was from very light to moderate intensity level of Borg's rate of perceived exertion (<40-60% HR max , RPE categorization) to avoid any complications that might arise. (Borg, 1998) Training sessions were conducted to the comfort of the participants.

2. Dietary variation among subjects could have influence on their physiological state. It was not possible to control the dietary pattern of the subjects as the diet within the environment was similar. It was assumed that the subjects fed on similar diet (carbohydrates as a major diet) throughout the period of training.

3. It was not possible to control the physical activity level of subjects outside their routine work. It was ensured that the subjects minimized being involved in any strenuous physical activity (especially cycling to school) that could affect the result during the training period.

4. Adherence to training was inconsistent. The initial twenty- five (25) participants that started the training reduced to seventeen (17) by the final day of test.

CHAPTER TWO

2.0 REVIEW OF RELATED LITERATURE

2.1 Introduction

Many components of metabolic syndrome are associated with overweight and sedentary lifestyle. Overweight people are more likely to be diabetic, hypertensive, and have higher cholesterol levels. Categorization of BMI for ideal weight shows that, ideal weight is less than 25kg/m^2; overweight is between 25 and 29.9kg/m^2; obesity class 1 is between 30 and 34.9kg/m^2; obesity class 2 is between 35 and 39.9kg/m^2, and extreme obesity is a BMI greater than 40kg/m^2 (Heyward, 1997; Baumgertner, Jackson, Mahar & Rowe, 2006). .

Studies have pointed out that physical training may be beneficial for the prevention and management of overweight and its complications (Sato, 2000; Borghout & Keizar, 2000; Lesnick, 2002;

America Diabetes Association, 2003). Abnormal or high serum glucose/ impaired glucose transport, hyperinsulinemia or insulin deficiency, aberrant lipid metabolism, particularly increased lipid availability, are implicated in the cause of T2DM in overweight persons (Lamonte, Blair, & Church, 2005; Dulloo, 2005; Shaibi, Robert, & Goran, 2008).

Since this study investigated the effect of aerobic training on serum glucose, insulin, glucagon, lipids and lipoproteins of overweight male adults, available literature was critically reviewed under the following subheadings:

2.2 Glucose transport and the role of exercise training on glucose metabolism

2.2.1 Experimental studies on the effect of exercise training on glucose transport and glucose metabolismin

2.3 Role of insulin on carbohydrate metabolism

2.3.1 Effects of exercise training on insulin sensitivity.

2.3.2 Effect of exercise on insulin resistance.

2.3.3 Experimental studies on the effects of exercise training on insulin, insulin sensitivity and insulin resistance

2.4 The role of glucagon on carbohydrate metabolism

2.4.1 Effect of exercise training on glucagon.

2.4.2 Experimental studies on the effect of exercise training on glucagon

2.5 The role of lipids in carbohydrates metabolism

2.5.1 Effects of exercise training on triglycerides

2.5.2 Effects of exercise training on cholesterol

2.5.3 Effects of exercise training on high density lipoprotein-cholesterol (HDL-C)

2.5.4 Effects of exercise training on low density lipoprotein- cholesterol

2.5.5 Experimental studies on the effects of exercise training on lipid (triglycerides, and cholesterol) and lipoproteins (low density lipoprotein and high density lipoproteins.

2.2 Glucose Transport And The Role Of Exercise Training On Glucose Metabolism

Glucose metabolism connotes various biochemical processes responsible for the formation, breakdown and inteconversion of carbohydrates in living organisms (Wildman & Miller, 2004; Williams, 2007). This is the process by which simple sugar found in many food are processed and used to produce energy (Williams, 2007). The regulatory mechanism for maintain glucose homeostasis (70-120mg/dl or 4-7.8mmol/l) in the body is the counter-regulatory action of insulin and glucagon. The major long – term effects of diabetes are caused by hyperglycemia where the plasma glucose concentration exceeds 120mg/dl (Roy & parker, 2010),

Glucose transport is the rate – limiting step in muscle glucose utilization and is carried out by the glucose transport protein present on the cell membrane (Goodyear *et al*; 1994; Dresner, Lauren & Maccuci, 1999). Insulin facilitates muscle glycogen synthesis (GS) through its action on both transport and glucose synthesis activity. Thus, an increase in insulin responsiveness results in a large increase in glucose transport in maximally effective insulin stimulus with a proportional upward shift of the dose response curve. Insulin stimulates translocation of glucose transporter proteins (GLUT-4) to the plasma, thereby enhancing glucose transport capacity (Simpson, Whitehead & James, 2001; Fisher et al; 2008). In an earlier study, it was found that muscle contractions increase glucose transport in the absence of insulin in frog sartorius muscle (Hollosy & Narahara, 1965).

Subsequent studies have established that contractions stimulate glucose transport in the complete absence of insulin (Wallberg-Henriksson & Holloszy, 1985), and that contraction and insulin stimulates glucose transport by separate pathway (Lee, Hansen & Holloszy, 1995; Lund, Holman, Schmitz & Peterson, 1995; Ye, Gulve, Rameh & Birnbaum, 1995). The initial steps in the pathways by which contractions stimulate glucose transport have been identified. One of them is the release of Ca^{2+} from the sarcoplasmic reticulum (SR) (Young, Garthwaite, Bayan, Cartae & Holloszy, 1991), resulting in activation of Ca^{2+}/calmodulin-dependent protein kinase (CaMK) II, which is the isoform of CaMK found in skeletal muscle (Wright, Hucker, Hollowszy & Han, 2004). Studies, using this approach have shown that inhibition of Ca^{2+} release from SR, or inhibition of CaMk, prevents the increase in glucose transport induced by Ca ^{2}+ (Wright *et al*; 2004; Wright, Geiger, Hollowszy & Han 2005). The other pathway involves the AMP activation protein kinase (AMPK), which is activated by the decrease in ATP and creatine phosphate and increase in AMP induced by contractions (Fisher et al; 2008). Of these pathways, the Ca^{2+} activated one appears to be the more important, because it functions in both fast-twitch and slow twitch muscle whereas the AMPK mediated mechanism functions only in fast-twitch muscle (Wright *et al*; 2005).

The cellular signals utilized to stimulate the translocation of the GLUT4 containing vesicles and the vesicular apparatus likely involve activation of phosphatidylinositol 3-kinase (P13K), AKt, and protein kinase-C at a proximal end and possible phospholipase D at a further distal step of the insulin signaling pathway (Emoto, Klarrhund, Waters, Hu, Buxton, Chwla & Czech, 2000; Kristiansen, Nielsen, Bourgoin, Klip, Franco & Richter, 2001; Simpson *et al*., 2001). The classical P13K cascade also seems to be involved in the regulation of GS, possibly through deactivation of glycogen synthase kinase 3 (GSK3) and activation of protein phosphatase-1 (PP1) (Cartae & Holloszy, 1990; Lawrence & Roach, 1997; Wotaszewski, Hiyaki, Hirshman, Michael, Dutresne, Kahn & Goodyear, 1999; Brady & Saltict, 2001).

The most developed insulin resistance is most likely influenced by physical inactivity and increased body fatness (Morley, 1999; Reavens, 2003). Insulin resistance is among the most pervasive

metabolic complications associated with obesity and is linked with the pathogenesis of chronic diseases, such as T2DM and cardiovascular diseases (Boule, Haddad, Kenny, Wells & Sigal, 2001; Facchini, Hu, Abbasi & Reavens 2001). Weight loss through caloric restriction is known to attenuate and even reverse insulin resistance (Ross, Dagnone, Jones, Smith, Paddas,Hudson & Jansen 2000; Assali, Ganor, Beigel, Shafer & Hershscovici, 2001; Jansen, Fortier, Hudson & Ross, 2002; Toledo, Menshikova, Azuma, Ralikova, Kelley, Ritov & Kelley, 2008), and adding an endurance exercise training programme ; to caloric restriction diet has been proposed to augment improvement in insulin sensitivity (Goodpaster, Katsiaras & Kelley, 2003;American Dietetic Association, 2005; Toledo, Meshikova, Ritov, Azuma, Badikova, Delany & Kelley, 2007; Kelley, 2012).

In general, patients with impaired glucose tolerance (IGT), a target group for T2DM prevention, are characterized by having sedentary lifestyle coupled with poor physical fitness and insulin resistance. Boushed et al; (2007), reported that mortality rate in middle aged IGT men was increased in lifestyle changes but that a long-term intervention program, with emphasis on dietary counseling and physical exercise might be successful.

The possible hypoglycemic benefits of physical activity were originally observed by Aristotle, and later re-advocated as a mainstay of treatment by Allen and Josln, in the early 1920s (Peirce, 1999). In addition to type 2 diabetes mellitus (T2DM) (Albright, Franz, Hornsby, Kriska, Ullrich, Venty, ACSM Position Stand, 2000; Sigal *et al*; 2006); management of many chronic diseases now includes regular exercise as part of a viable treatment plan (American College of Sports Medicine (ACSM) *et al*; 2009; Kelley & Good, 2011). As scientists continue to work to elucidate the mechanism involved in glucose reduction, clinicians continue to translate bench-work into practical methods for treating the millions of patients afflicted with T2DM. Exercise is now well supported as an effective prescription for patients with high serum glucose or T2DM, acting therapeutically both acutely and chronically (Albright et al; 2000; Hu & Manson, 2003; Sigal *et al*; 2006; ACSM *et al*; 2009). It has been shown that an acute bout of SUBEX can lower blood glucose concentration for 2 to 48 hours post exercise (Edelmann, Staudner

&Bachmann, 1986; Albright et al; 2000; Hawley & Lessard, 2008), and improve insulin sensitivity up to 72 hours after cessation of any given exercise bout. ACSM, *et al*; (2009); recommended that patients with T2DM engage in total of 100 kcal/week of energy expenditure (3-5 days of exercise per week), mostly in the form of low to moderate (40-70% of Vo_2 max) exercise (Albright et al; 2000). The American Diabetic Association, (2003); Sigal et al; (2006), currently recommend 150m/week of exercise at an intensity of 40-60% Vo_2 max, no less than three days a week, and never with more than two consecutive days without physical activity.

Several studies (Coggan, 1991; Rogers, Yamamoto, King, Hagberg, Ehsani & Holloszy, 1988; Fisher, Gao, Han, Holloszy & Nolte, 2008), demonstrated that improvements in glucose tolerance and reduction in insulin resistance can be obtained in patients with T2DM after only one week of daily exercise at 80% of Vo_2 max. Kang, Robertson, Hagbert, Kelley, Goss, Dastiva, Sumunski & Utter (1996), reported that improvement in insulin sensitivity of patients with T2DM were achieved after one week of exercise at 80% Vo_2 max but not 50% $V0_2$ max (calorically matched).

Regular physical exercise improves reduced insulin sensitivity in lifestyle-related diseases including T2DM, hypertension, hyperinsulinemia and ischemic coronary disease (Skyler, 1998; American Dietetic Association, 2005, Holloszy, 2013). Several authors agree that continued physical training may be beneficial for prevention and management of these diseases (King & Kriska, 1992; Department of Health and Human Services, 1996; Sato, 2000; Borghouts & Keizer, 2000; American Diabetic Association, 2003). In high serum glucose, physical activity may improve insulin sensitivity and assist in diminishing elevated blood glucose levels into the normal range (70-120mg/dl) (Sato, 2003; Kelley, 2012). Recent studies strengthen the importance of long-term physical activity program for the treatment and prevention of hyperglycemia, a common metabolic abnormality and its complications (Tuomilehto, lindstrom, Erickson, Valle, Hamaleinen Hanne-Parikka, Keinanen-Kukaanemi, Laakson, Louheranta, Rastas, Salminen & Uusitupa, 2001; American Diabetes Association, 2004; Abbasi, Mclaughlin Lamndola & Reveans, 2006; Chris, 2012).

Studies (American Diabetes Association, 2004; 2006; Roy, 2007), have reported that there are consistent beneficial effects of regular physical activity on carbohydrate metabolism and insulin sensitivity, which can be maintained for at least 5 years when physical activity regiment were used at an intensity of 50-80% Vo_2 max three to four times a week for 30-60 minute a session. Improvements in glycelated hemoglobin (HbAic) were generally 10-20% of baseline and most marked in patient with mild T2DM and in those who are likely to be the most insulin resistance. Improvements in insulin sensitivity, hyperlipidemia and glucose transport/glucose tolerance are steps towards managing T2DM.

A great deal of evidences have shown support for exercise training in reducing glucose levels as an ideal factor in the management of T2DM (Zinman, 1990; Taunton & Mccargarl, 1995; Boule et al; 2001; Tansey, Tsalikian, Beck, Marcus, Buckinham, Weinzimer, Janz, Kollman, Xing Ruedy, Steffes, Borland, Singh, Tauborlane, & Diabetic Research Children Network (Directnet) Study Group; 2006; Khoo, Wallis, Tsentzas, Macdonald & Mansell, 2010; Yatsumbara, Tobina, Shido, Tokuyama & Tanaka, 2010). Diabetes Prevention Programme Research Group, (2002), documents that with lifestyle modification (weight loss, regular moderate physical activity), diabetes can be delayed or prevented. With exercise and nutrition T2DM can be managed (Lintenberg, Hoekstra, Bol, Zonderland & Erkelens, 1997; Ciccone, 2002). It is becoming increasingly clear that the epidemic of T2DM sweeping the globe is associated with decreasing levels of physical activity and an increasing prevalence of obesity. The importance of promoting physical activity as a vital component of prevention as well as management of T2DM must be viewed as a high priority (King & Kriska, 1992; American Association of Diabetes, 2003, Colberg & Greico, 2009).

Because clinicians are now relying more on exercise prescription to manage major metabolic disorders like T2DM in overweight, it is imperative that physicians understand the normal blood glucose changes during SUBEX (Goodwin, 2010).

2.2.2 Experimental Studies On The Effect Of Exercise Training On Glucose Transport And Glucose Metabolism

Insulin action on glucose transport is characterized in terms of insulin sensitivity and insulin responsiveness (Kahn 1978). Insulin responsiveness is defined in terms of the increase in glucose transport induced by a maximally effective insulin concentration.In a study on the role of exercise in reducing the risk of diabetes and obesity-exercise-induced increase in muscle insulin sensitivity. Holloszy, (2013), reported that the increase in muscle glucose transport induced by exercise is independent of insulin. As the acute effect of exercise on glucose transport wears off, it is replaced by an increase in insulin sensitivity. An increase in insulin sensitivity results in a shift in the insulin dose-response curve to the left, with a decrease in the concentration of insulin needed to induce 50% of the maximal response. This phenomenon, which plays a major role in rapid muscle glycogen accumulation after exercise, is not mediated by amplification of the insulin signal. The effect of exercise on muscle insulin sensitivity is mimicked by hypoxia and by treatment of muscle with 5-aminoimidazole-4-carboxamide-1-1 β-D-ribofuranoside to activate AMP activated protein kinase. The post-exercise increase in sensitivity of muscle glucose transport to activation is not specific for insulin but also involves an increased susceptibility to activation by a sub maximal contraction/hypoxia stimulated. The increase in insulin sensitivity is mediated by translocation of more GLUT-4 glucose transporters to the cell surface in response to a sub maximal insulin stimulus.

Depletion of muscle glycogen by exercise is followed by an enhanced ability to synthesize glycogen (Bergstrom & Hultman 1966; Roch- Norlude, Bergstrom & Altman, 1972). In a study by Fell,Terblanche,Ivy, Young & Hollowszy, (1982), of this phenomenon, it was found that the rates of insulin stimulated glucose uptake and glycogen synthesis were higher in perfuse muscles of rats, 18 hr. after exercise when glycogen levels were kept low than when glycogen levels were raised by carbohydrate feeding. It was not clear whether this persistent effect of exercise was due to a persistent increase in insulin action or to a persistence of the exercise-induced insulin independent increase in glucose transport that was additive to the effect of insulin. A follow-up experiment was performed by Young, Garthwaite, Baya, Cartier & Hollowszy, (1983), on how carbohydrate-feeding speeds reversal of

enhanced glucose uptake by muscle after exercise. Rats were exercised to deplete glycogen, and glucose uptake by per fused muscles measured 60 min and 18h after exercise in the absence of insulin. Glucose uptake was markedly increased 60 min after exercise. Eighteen hours later, only 50% of the increase in glucose uptake had worn off in rats fed carbohydrate-free diet, whereas the increase in uptake had completely reversed in rat fed carbohydrate to raise muscle glycogen. Because there was no insulin in the perfusion medium, they erroneously attributed the persistent increase in glucose uptake 18h after exercise to a slowing of reversal of the exercise-induced insulin-dependent increase in glucose uptake as a result of prevention of glycogen repletion.

Subsequent studies on muscles incubated in vitro showed that the increase in muscle glucose transport induced by exercise reverses within 2-3 hr even in the absence of glycogen repletion (Gulve *et al*; 1990; Ploug, Galbo, Vinten, Jorgensen & Richter, 1987, Young, Wallberg-Henriksson, Sleeper & Hollowszy, 1987). Young *et al*; (1987), in a study titled ‘‘reversal of the exercise-induced increase in muscle permeability to glucose’’, reported that incubation of muscle with 33% rat serum or a very low concentration of insulin 7.5 μu/ml, appeared to markedly slow reversal of the increase in glucose transport. The increase in glucose transport observed by Young *et al;* (1983), 18 hours after exercise in muscles perfuse with insulin-free medium was likely due to the markedly bound to the muscle insulin receptors and to an increase in GLUT-4 glucose transporter induced by exercise.

In light of the evidence that glycogen depletion enhances and glycogen super-compensation reduces insulin action (Fell *et al*; 1982; Zorzano, Balon, Goodman & Ruderman, 1986. Cartee, Young, Sleeper, Zaerath, Walberg-Henriksson & Hollowszy, (1989), compared the effects of a high-carbohydrate diet and a carbohydrate-free diet on persistence of the increase in muscle insulin sensitivity after exercise. Three hours after exercise, insulin sensitivity of glucose transport was increased in epitrochlearis muscle in both carbohydrate fed and fasted rats. However, 18h after exercise, the increase in insulin action had completely reversed whereas it persisted for at least 48h in rats fed carbohydrate-free diet.

Insulin facilitates muscle glycogen synthesis (GS) through its action on both glucose transport and on GS activity. Insulin stimulates translocation of glucose transporter proteins (GLUT-4) to the plasma membrane, thereby enhancing the glucose transport capacity (Cartee Holloszy, 1990; Simpson *et al*; 2001).

The sensitivity of muscle glucose transport to stimulation by various other agents is also markedly increased (Cartee & Holloszy, 1990). Cartee & Holloszy (1990) in a study titled "Exercise increases susceptibility of muscle glucose transport to activation by various stimuli, observed that the activation of muscle glucose transport by 20 min of hypoxia, a sub maximal stimulus, is greatly amplified in epitrochlearis muscle 3hr after exercise. The concluded that sensitivity of glucose transport to hypoxia, as well as to insulin increase after exercise, provides evidence that a late step that is common to the insulin and contraction/hypoxia-stimulated pathways is involved in mediating the increase in sensitivity In general, patients with impaired glucose tolerance (IGT), a target group for T2DM prevention, are characterized by having sedentary lifestyle coupled with poor physical fitness and insulin resistance (Morley, 1999). Randomized controlled intervention trials (RCT) in Norway (Torjesen, Burkeland, Anderson, Hjermannn, Holme & Urdal, 1997) and China (Pan, Lillioja, Kriketos, Milner, Baur, Bogardus, Jenkins & Storhen, 1997) showed that diet and/or exercise intervention led to a significant decrease in the incidence of diabetes among those with IGT,.

The Finish Diabetes Prevention Study (Tuomelhto *et al*; 2001) demonstrated that the risk of diabetes from IGT was reduced by 58% in the intervention group that received individualized counseling, which aimed to reduce the total intake of fat and increase the intake of fiber and the level of physical activity. The reduction in the incidence of diabetes was directly associated with changes in lifestyle, leading them to conclude that T2DM could be prevented by changes in lifestyle of high-risk subjects.

Recent results of Diabetes Prevention Program Research Group, Knower, Barrett-Connore, Fowler, Hamman, Lachin, Walker &Nathan, (2002), are more impressive. Impaired Gluccose Transport

persons (mean body mass index: 34.0) were randomly assigned to placebo, Metformin (850mg twice daily), or a lifestyle modification program with the goal of at least a 7% weight loss and physical activity of moderate intensity, such as brisk walking, for at least 50 min per week. After an average follow-up for 2.8 years the lifestyle intervention reduced the incidence of diabetes by 58% and metformin by 31% as compared with placebo. They concluded that lifestyle changes and treatment with metformin reduced the incidences of diabetes in IGT persons and that lifestyle intervention was more effective than metformin.

The principal purpose of physical exercise for the primary prevention and treatment of lifestyle-related diseases is to improve insulin resistance (Betaman, Start, Willis, Houmard & Kraus, 2011). During physical exercise, the glucose uptake by the working muscles rises 7 to 20 times over the basal level, depending on the intensity of the work performed. Intense exercise provokes the release of insulin-counter regulatory hormones such as glucagon and catecholamine, which ultimately cause a reduction in the insulin action (Sato, 2000).

To evaluate the effect s of mild physical training (Walking) combined with diet therapy (1000-1600 Kcal/day) on insulin sensitivity in obese patients with type 2diabetes, Yamanouchi, Shinozaki, Chikada, Nishkawa, Ito, Shinizu,Suzuki, Maeno, Kato,Oshida & Sato, (1995) performed the following studies. Subjects were divided into two groups, 10 patients were treated by di*et al*one (Group D) and 14 patients practiced dietary restriction and walking at least 10,000 steps/day monitored by Pedometer (GroupDE [diet and exercise], 19,200 $\pm$ 2, 100 steps/day). Group D was instructed to maintain a normal daily routine (4500 $\pm$ 290 steps/day). After an intervention period of 6 to 8 weeks, body weight (BW) in both groups was significantly decreased, and glucose infusion rate (GIR) in group D did not change markedly, while it increased significantly in group DE. A significant correlation was observed between DMCR (DMCR represents the positive changes in metabolic clearance rate of glucose (MCP) after training) and average daily steps ($r = 0.7257$, $P < 0.005$). Another DBW (DBW represents BW reduction after training) suggest that walking, which can be safely performed and easily incorporated into daily

life, can be an adjunct therapy to diet treatment in obese type II diabetic patients, not only for reducing BW, but also for improving insulin sensitivity.

Although data suggest that physical activity is associated with decreased insulin resistance, recommendations for exercise training are not specific for age or level of obesity. Therefore Coker *et al*; (2006), examined the influence of moderate-intensity (MI) (50% of Vo2 max) exercise training versus high-intensity (HI) (75% of Vo2 max) exercise in training on insulin-stimulated glucose disposal (ISGD) in elderly individuals. The following medical examinations, 21 overweight (BMI = 21 $\pm$ 1kg/m2) elderly (74 $\pm$ 1 yr) subjects were randomized to 1,H1, 2, M1 or 3, non-exercising control groups subjects enrolled in H1 or M1 completed a 12wk exercised training regimen designed to expand 1000k cal/wk^{-1}. ISGD was assessed using a hyperinsulinemia, euglycemic clamp pre- and post- intervention. ISGD was corrected for hepatic glucose production (glucose Ra) using a constant rate infusion of [6.6-2 H2] glucose and determined during the last 30 min of the clamp by subtracting glucose Ra from the exogenous glucose infusion rate. Non oxidative glucose disposal was calculated using indirect calorimetry. Body composition testing was completed using dual energy x-ray absorptionmetry. Results indicated ISGD increased by approximately 20% with H1 (ΔO) 1.4 $\pm$ 0.5 mg kg^{-1} FFM min^{-1}). However, ISGD did not change (Δ of – 0.4 $\pm$ 0.1 mg/ kg^{-1} FFM: min^{-1}) in the control group. Non oxidative glucose disposal increased with H1 (/\ of 1.4 $\pm$ 0.4 mg. kg^{-1} FFM min^{-1}), but there was no change in non oxidative glucose disposal with M1 in the control group. No change in body weight or percentage of body fat was observed in any group. It was concluded that in weight-stable subjects, M1 resulted in no change in ISGD, and the improvement in ISGD with H1 was completely reliant on improvements in non oxidative glucose disposal.

Jentjen,s, Veriables & Jeukendrup, (2004), investigated whether combined ingestion of two carbohydrate (CHO) are absorbed by different intestinal transport mechanisms would lead to exogenous CHO oxidation rates of > 1.0 g/min. Nine trained male cyclists (Vo_2 max 64 $\pm$ 2 ml. kg body wt^{-1} min^{-1}) performed four exercise trials, which were randomly assigned and separated by at least 1 wk.

Each trial consisted of 150 min of cycling at 50% of maximal power output (60 ± 1% Vo2 max), while subjects received a solution providing either 1.8 g/min of glucose (GLU) 1.2gm,in of glucose ± 0.6g/min. of sucrose (Glu ± Suc.) 1.2g/min of glucose 0.6 g/min of maltose (Glu - Mal), or water. Peak exogenous CHO oxidation rates were significantly higher ($P < 0.05$) in the GLU ± SUC trial (1.25 ± 0.079/min) compared with the GLU and GLU -Mal trials (1.06 ± 0.08 and 1.06 ± 0.06 g/min respectively). No difference was found in (peak) oxogenous CHO oxidation rates between GLU and GLU - Mal. These results demonstrate that when a mixture of glucose and sucrose is ingested at high rates (1.8g/min) during cycling exercise, exogenous CHO oxidation rates reach peak values of -1.25g/min.

It is apparent that any physical stress imposed on the body that requires an increase in muscle metabolism and at least some subsequent utilization of blood glucose obligatorily requires strict glucose regulatory mechanisms (Coker & Kjaer, 2005; Godwin, 2010). The effect of exercise on the improvement of the metabolic profile has been controversial so far, but combination of dietary restriction and regular physical exercise might be effective in delaying or preventing type 2diabetes.

Regulation of plasma glucose concentration for type 1 diabetic patients is challenging, and exercise is an added complication. From a metabolic prospective, the significant exercise – induced effects are increased glucose uptake rate by the working tissues, increased hepatic glucose release to maintain overall glucose homeostasis, and decreased plasma insulin concentration. During prolonged exercise, glucose levels dropped significantly because of the decrease in hepatic glucose production. With the long-term goal of developing a close-loop insulin delivery system operating under various physiological conditions, it is necessary to develop a model that is capable of predicting blood glucose concentration at rest and during physical activity. It is in this light that Roy & Parker (2007) examined the dynamic modeling of exercise effects on plasma glucose and insulin levels. A minimal model developed previously was extended to include the major effects of exercise on plasma glucose and insulin levels. Differential equations were developed to capture the exercise-induced dynamics of plasma insulin clearance and the elevation of glucose uptake and hepatic glucose production rates. The

decreasing liver glucose output resulting from prolonged exercise was modeled using the equation depending on exercise intensity and duration. Results indicated that the exercise model successfully captured the glucose insulin dynamics during short- and long- term exercise. Model predictions of glucose and insulin dynamics during the post exercise recovery period were also consistent with literature data. They concluded that the model successfully emulated the physiological effect s of exercise on blood glucose and insulin levels. This extended model may provide a new disturbance test platform for the development of closed-loop glucose control mechanisms.

To examine the acute glucose-lowering effects of aerobic exercise in children and adolescents with type 1 diabetes, Tansey *et al*; (2006) investigated the effects of aerobic exercise on glucose and counter regulatory hormones concentrations in children with type 1 diabetes. Fifty children and adolescents with type 1 diabetes (age 10 to < 18 years) were studied during exercise. The 75-min exercise session consisted of four 15-min periods of walking on a treadmill to a large heart rate of 140 bpm and three 5-min rest periods. Blood glucose and plasma glucagon, cortisol, growth hormone, and nor epinephrine concentrations were measured before, during and after exercise. Results indicated that in most subjects (83%), plasma glucose concentration dropped at least 25% from baseline and 15(30%) subjects became hypoglycemic (< 0r = 60mg/dl) or were treated for low glucose either during or immediately following the exercise session. The incidence of hypoglycemia and/or treatment for low glucose varied significantly by baseline glucose, occurring in 88 vs. 13 (6%) of subjects with baseline values < 120 – 180, and 180 mg/dl, respectively (P < 0.001). Exercise-induced increases in growth hormone and nor epinephrine concentrations were marginally higher in subjects whose glucose dropped < or = 70mg/dl. Treatment of hypoglycemia with 15g of oral glucose resulted in only about a 20-mg/dl rise in glucose concentration. They concluded that in youth with type 1 diabetes, prolonged moderate aerobic exercise results in a consistent reduction in plasma glucose and the frequent occurrence of hypoglycemia when pre-exercise glucose concentrations are <120 mg/dl. Moreover,

treatment with 15g of oral glucose is often sufficient to reliably treat hypoglycemia during exercise in these youngsters.

The recent Surgeon General's Report on Physical Activity and Health (Department of Health and Human services, 1996), recommended that individuals accumulate 30 min of moderate physical activity on most days of the week. In the context of diabetes, it is becoming increasingly clear that the epidemic of type 2diabetes sweeping the globe is associated with decreasing levels of activity and an increasing prevalence of obesity. Thus, the importance of promoting physical activity as a vital component of the prevention as well as management of type 2diabetes must be viewed as high priority. It must also be recognized that the benefits of physical activity in improving the metabolic abnormalities of type 2 diabetes is probably greatest when used early in its progression from insulin resistance, to impaired glucose tolerance, and to overt hyperglycemia requiring treatment with oral glucose-lowering agents and finally insulin. For people with type 1 diabetes, the emphasis must be on adjusting the therapeutic regimen to allow safe participation in all forms of physical activity consistent with an individual's desires and goals.

Hypoglycemia during physical activity rarely occurs in non-diabetic individuals. The metabolic adjustments that preserve normoglycemia during physical activity are in large part hormonally mediated (American Diabetic Association 2004). The benefits of exercise for the management of diabetes and obesity might originate from increased lipid oxidation in response to training adaptation (Hawley, Brouns & Jeukendrup, 1998). In order to prevent major health complications in hyperglycemia, it is important to maintain the plasma glucose concentration within the normoglycemic in range. A number of studies in adults have demonstrated that regular moderate exercise improves insulin sensitivity and reduces the risk for cardiovascular disease, type 2 diabetes and some types of cancer.

2.3 Role of Insulin in Carbohydrate Metabolism

Insulin is a polypeptide with 5.1 amino acids and a molecular weight of 580gms. Insulin is secreted in the islet of Langerhan by the beta cells of the pancreas. Basal level of insulin in plasma is 10µm/ml. Its biological half-life is 10 minutes (Maninen, 2004; Sembulingan & Sembulingan, 2010). The net effect of insulin is storage of carbohydrate, protein and fat (Maninen, 2004). It is the most important hormone that regulates the level of glucose in the blood, the rate of its absorption, and its conversion to glycogen (Ochei & Okolhalkar, 2007). Insulin operates to store fuel (Brooks, Faley, & Baldwin 2005; Plowman and Smith, 2008; Powers & Howley, 2012). Insulin facilitates the uptake and utilization of glucose (facilitated diffusion) by various tissues in the body, most notably, the muscle and adipose tissues (Defronzol, Jucol, Jequer, Maeder, Walmren & Felber, 1981; Williams, 2007).

Insulin is the only anti-diabetic hormone secreted in the body. Insulin reduces blood sugar level by increasing transport and uptake of glucose by the cells, promotes storage of glucose inhibits glycogenolysis, promotes peripheral utilization of glucose by immediate oxidation of glucose that enters the cell, inhibits gluconeogenesis and prevents the formation of glucose from proteins by inhibiting the release of amino acids from muscles (Dela, Larsen, Mikines, Plough, Peterson & Galbo 1995; Rorsman 2005; Sembulingan & Sembulingan, 2010).

Insulin stimulates translocation of glucose transporter protein (GLUT-4) to the plasma membrane, thereby enhancing the glucose transport capacity (Kristiansen et al; 2001). Insulin enhances the activity of glucose synthesis by decreasing phosphorylation of the enzyme (Cohen, 1993). The classical phosphatidylinositol 3 kinase (P13k) cascade also seems to be involved in the regulation of glucose synthesis, possibly through deactivation of glycogen synthase kinase 3 (P13K) and activation of protein phosphate-1 (PP-1) (Wojtaszewski, Hassen, Kliens & Richter, 1997; Hassen, Nolte, Chen & Hollowszy, 1998; Wojtaszewski, Hassen, Gade, Kleins, Markuns, Goodyear & Richter, 2000; Wojtaszweski, Nielsen & Richter, 2002).

Insulin and glucagon are hormones that work to regulate the level of sugar in the body and to keep it under a healthy range. The coordinated action by insulin and glucagon shows that an increase in

insulin level inhibits glucagon release from alpha cells. This paracrine effect is a basic element in insulin control of glucagon activation of both hepatic gluconeogenesis and lipolysis in adipose tissue (Galbo , Holst & Christensen, 1972; Galbo, 1983; Rorsman, 2005). Consumption of carbohydrate triggers release of insulin from beta cells. Alpha cells become inhibited and cease to secrete glucagon. These actions produce a rapid return to fasting blood sugar levels and storage of glucose as glycogen and lipids (Galbo , Richter, Hilsted, Holst, Christensen & Henrikson, 1977; Wolfe *et al*; 1986; Kang et al; 1996).

In order to prevent major health complications, it is important to maintain the plasma glucose concentration within the normoglycemic range (4-7.8mmol/l or 70-120mg/dl) (Diabetes Control and Complications Trial Research Group, 1993, 1996). The major long-term effects of diabetes are caused by hyperglycemia, where the plasma glucose concentration exceeds 120mg/dl. In order to achieve tighter glucose control, there is the focus on the synthesis of an automated insulin delivery system composed of a continuous glucose device and an insulin pump (Parker, Doyle & Peppas, 1999; Hovorka, Conanico, Chassin, Haveter, Massi-Benneditti, Orsin-Federia, Pieber, Schaller, Schaupp, Vering & Willinska, 2004; Roy & Parker, 2010).

2.3.1 Effect of Exercise Training On Insulin

Exercise plays an important role in regulating insulin within the body. With exercise, insulin is not readily released from pancreas due to the lowered blood glucose levels. This self regulation allows the body to not require insulin injection (Normal Regulation of Blood Glucose Levels 2002; Ciccone, 2002). During exercise the perfusion of the muscle is dramatically increased compared with at rest, in this way, the delivery of insulin (Plasma flow x plasma insulin concentration) is markedly enhanced during exercise even when plasma insulin concentration are reduced by up to 50% during exercise (Woftaszewski *et al*; 2002; Lamonte et al; 2005). Insulin is the principal hormone involved in the uptake and storage of glucose and FFA, and glucagon to cause the mobilization of those fuels from storage as well as increase gluconeogenesis. Given that insulin is directly involved in the uptake of glucose into tissue and that glucose uptake by muscles can increase seven-twentyfold during exercise (Felig &

Wahren, 1975; Bent, 1986; Kang et al; 1996,), insulin concentration decreases during exercise of increasing intensity (Pruett, 1970; Hartley, Mason, Hoggan, Jorus, Kofchen, Mougey,Wherry, Pennington & Richter, 1972; Galbo, holst, & Christensen, 1975; Krishna, Coker, Lacy, Zinker, Halsetti & Wasserman, 2013), this of course, is an appropriate response. If exercise were associated with increase insulin, the plasma glucose would be taken up into all tissues (including adipose tissues) at faster rate, leading to an immediate hypoglycemia. The lower insulin concentration during exercise favors the mobilization of glucose from the liver and FFA from adipose tissue, both of which are necessary to maintain glucose concentration.

The positive influence of exercise training on insulin action has been reported in numerous investigations (King, Dalsky & Cutter, 1988; Mikines, Sonne, Triorier & Galbo, 1989; Dela, Mikines, Linstow, Secher & Galbo, 1992; Muhammad, 2003, Christ-Roberts, Pratipanawatr, Barria, Delport, Kashyap & Mandarino, 2004; Boule, Weisnage & Likka, 2005). The critical role in the efficacious treatment of insulin resistance has been reported by Coker & Kjaer, (2005), to be dependent on intensity, duration and frequency of aerobic exercise training. Several studies have expressed various conclusions on the effect of exercise training on insulin. Wolfe *et al;* (1986), in a simulation study of mild exercise (P $V0_2$ max = 40) for 60 minutes to evaluate the physiological effects of exercise on plasma insulin concentration, reported a decline from basal level (12.2 μm/ml) with the onset to the end of exercise. They also reported that insulin concentration climbed back to its basal level during the recovery period. In normal subjects, there is small hyperglycemic response during exercise that increases substantially immediately at exhaustion and persists for up to 1 hour. This is accompanied in recovery by hyperinsulinemia (Marlis & Vranie, 2002). The prior exercise enhanced insulin-stimulated glucose utilization in human was first reported by Devlin, Hirshman, Horton & Horton, (1987).

Proirier, Tramblay, Broderick, Catellier, Tancred & Nadeau, (2002), reported that non obese subjects with type 2 diabetes showed an increase in insulin sensitivity due to impact of moderate aerobic exercise training on insulin sensitivity. Prolonged exercise induces several fundamental metabolic

changes in the body (Wasserman, Gree, Williams, Lacy & Abeembrad, 1991). Elevated physical activity promotes a drop in insulin concentration from its basal level (Felig & Wahren, 1975). Zalic, Moss, Niger & Looyon, (2001), reported that 10 weeks of physical activity intervention, significantly decreased fasting insulin in 194 boys and girls.

2.3.2 Effect of Exercise Training on Insulin Sensitivity

Insulin action on glucose transport is characterized in terms of insulin sensitivity and insulin responsiveness (Kahn, 1978; Mcauley, Williams, Mana, Goulding, Chisholm, Wilsom, Story, Melay, Harpes & Jones, 2000). Insulin sensitivity is defined in terms of the concentration of insulin required to cause 50% of its maximal effect on glucose transport. An increase in insulin responsiveness results in a large increase in glucose transport in response to a maximally effective insulin stimulus, with a proportional upward shift of the dose response curve. Insulin sensitivity is the first order constant for the disappearance rate of glucose (K_{rTT}) (Bonora, Moyhutte, Zankanaro, Cigolini, Querena & Cacciatore, 1989).

That exercise increases the sensitivity of the glucose transport process to insulin in skeletal muscle, was first discovered by Richter, Garatto,, Goodman & Ruderman, (1982), in Neil Ruderman's laboratory. In an earlier study, it was found that muscle contractions increase glucose transport in the absence of insulin in frog sertoritis muscle (Holloszy, 1965). The benefit of exercise for the management of diabetes and obesity might be increased lipid oxidation in response to training adaptation (Delkin & Ruderman, 2002; Diabetes Prevention Research Group, 2005,).

Studies on the mechanisms by which increase in muscle insulin sensitivity is mediated, show that insulin, muscle contraction, and hypoxia, all induce increase in muscle glucose transport by stimulating movement of GLUT-4 from intracellular storage sites to the cell surface (Holloszy & Hassen, 1996; Hassen et al; 1998). It has been suggested that, the addition to GLUT-4, insulin increases the intrinsic activity of the GLUT-4 at the surface of muscle cells

(Sweeney, Somwar, Pamlal, Volchuk, Leyama & klip 1999, Somwar, Perreault, Kapur, Taha, Sweeney, Ramlal, Kim, Keen, Gote, Klip & Marette, 2000; Kristiansen et al; 2001). It has been shown using the same protocol that unlike increase in insulin sensitivity, the response of glucose transport to a maximal stimulus is not augmented 3 hours after exercise (Gulve *et al*; 1990). There has been much interest in the possibility that the increase in insulin sensitivity after exercise is mediated by an amplification of the insulin signal (Hadda & Adams, 2003; Heled, Shapiro, Shani, Maran, Langzam, Barash, Sampson & Mayeovital, 2004). There is the evidence that the increase in sensitivity is not specific for insulin but that it also involves increased sensitivity to agents that activate glucose transport via the contraction/hypoxia-stimulated pathway (Cartee & Holloszy, 1990; Fisher, Gao, Han, Holloszy & Nolte, 2002). The increase in insulin sensitivity is mediated by a mechanism that lies downstream of the insulin-signaling and contraction/hypoxia-signally pathway. An increase in insulin sensitivity could be mediated by movement of a larger proportion of the GLUT4 that are available for translocation into regions in which the insulin signals are strongest (Kristiansen et al; 2001).

On insulin sensitivity, several studies reported an increase in response to different exercise programs (Trueth, Hunter, Figueron-Colon & Goran, 1998; Gutin & Owens, 1999; Gutin, Barbeau, Owens, Lemmon, Bauman, Alisson, Kang & Litaka, 2002; Nassis, Papapntakou, Skenden, Triandafiillopoulou, Kavouras, Yanakaoulia, Chrousos & Siclosis,2005; Shaibi *et al*; 2006; Bell, Watts, Sinfarikas, Thompson, Ratnam, Bulsara, Finn, O'doiscoll, Green,Janes & Davis, 2007). Van der Heijden et al; (2009), reported significant increase in peripheral and hepatic insulin sensitivity in both lean and obese sedentary adults. Several studies have shown that prolonged exercise increased insulin sensitivity (Romijn et al., 1993; Holloszy, 2005; Guyton & Hall, 2006; 2011), which has been shown to promote glucose transport. These studies have shown that increased glucose transport due to exercise is not only due to increase in insulin sensitivity but also due to muscle contraction and hypoxia. They have also shown that the

increase in sensitivity is not just to insulin but also to stimulation of glucose transport by the contraction/hypoxia pathway, and is mediated by translocation of more GLUT4 to the cell surface from the cell interior in response to sub-maximal stimulus (Hassen et al; 1998).

A number of studies in adults have demonstrated that regular moderate exercise improves insulin sensitivity and reduces the risk of cardiovascular disease, type 2 diabetes and some types of cancer (Greiwe, Hickner, Hassen, Racette, Chen & Holloszy, 1999; Manson, Nathan, Krolewski, Stenpter, Willet & Hennekens, 1999). Improved insulin sensitivity has been shown in children and adolescents in response to various exercise training programs (Treuth *et al*; 1998; Gutin & Owens, 1999; Gutin *et al*; 2002; Nassis *et al*; 2005; Shaibi *et al*; 2006; Bell *et al*; 2007).

Other studies have established the role of exercise training in enhancing insulin sensitvity. King, Albert & Herman, (1998), reported that improvements in insulin sensitivity of patients with type 2 diabetes was achieved after one week of exercise at 70% Vo_2 max, which suggests that short term effect of exercise on insulin sensitivity might be mediated through glycogen depletion. Because improved insulin sensitivity from an exercise bout lasts no more than 72 hours (Simoneau, Colberg, Thaete & Kelley, 1995; Sigal *et al*., 2006; Golbert & Grieco, 2009), it is critical that patients maintain regular exercise schedule. It has been hypothesized that enhancing oxidative capacity via endurance exercise training may be responsible for most of the improvement in insulin sensitivity after exercise training – weight loss program (Goodpastor, Katsiaras & Kelley, 2003, Berggren, Hulver, Dohm & Houmard, 2004; Toledo *et al*; 2007; Toledo, Menshikova, Azuma, Railikova, Kelley, Ritov & Kelley, 2008). Although, improvement in insulin sensitivity after weight loss in obesity appears to occur independently of changes in skeletal muscle fatty acid oxidation, oxidation capacity, mitochondrial function or mitochondrial size (Berggren, Boyle, Champman & Houmard, 2008; Toledo *et al*; 2008). Data from studies examining the effect of exercise training/weight program on insulin sensitivity are further complicated because weight loss or reduction in fat mass can reduce systemic fatty acid mobilization (Klein *et al*., 1996; Lofgren, Holfstedt, Ryden, Thorne, Holmwahenberg & Arner,2002), which can itself

improve insulin sensitivity (Bajaij, Suraaornkul, Romanejji,Cline, Mandarino,Shulman & Defrozo,2005). Studies by Ross, Dagnone, Jones, Smith, Paddass, Hudson & Jansen, (2000); Dekker, Lee, Hudson, Kilpatrick, Graham, Ross &, Robinson, (2007) have demonstrated that exercise training, and a resultant increase in oxidation capacity does not improve insulin sensitivity when subjects do not lose weight.

Other studies have shown that muscle triglycerides content is inversely related to insulin sensitivity (Simoneau, Colberg, Thaete & Kelley, 1995; Goodpaster, Thaete, Simoneau & Kelley, 1997; Pan, Lillioja, Kriketos, Milner, Baur,Bogardus, Jenkins & Storhen, 1997), suggesting that lower intensity exercise are effective for increasing insulin sensitivity. Landt, Campaigne, James & Sparling, (1985) investigated the effects of exercise training on insulin sensitivity in adolescents, with type I diabetes and reported that insulin sensitivity assessed via euglycemic clamp technique at insulin infusion rates of 100 µm/m2/min showed an increase in insulin mediated glucose disposal from 274 + 33 to 338 $\pm$28 mg/m2/min, representing an increase of insulin sensitivity of 23+ 5% ($P< 0.01$).

Studies have shown that through moderate intensity aerobic exercise training, insulin sensitivity can be improved thereby enhancing proper metabolism of carbohydrate. Considerable information regarding the post-exercise increase in insulin sensitivity phenomenon has accumulated since it was first reported by Riderman's group in 1982. Holloszy, (2005), reported that the increase in sensitivity is not just in insulin but also to stimulation of glucose transport by the contraction/.hypoxia pathway; the increase in sensitivity is mediated by translocation of more GLU T-4 to the cell surface in response to a sub maximal stimulus; it requires the presence of serum during the period of stimulation by contraction, hypoxia, or AICAR; and the increase in sensitivity does not require protein synthesis.

2.3.3 Effect Of Exercise on Insulin Resistance

Insulin resistance is a physiological abnormality that increases the likelihood that one or more of the abnormalities will be present. Such abnormalities include compensatory hyperinsulinemia or some degree of glucose intolerance, such as impaired fasting glucose,

dyslipidemia, such as increased triglycerides, decreased high density lipoprotein-cholesterol (HDL-C), and increased low density lipoprotein (LDL) (Bells, Chmitz-peiter, Lim-Traser,Bedin, Cooney, Kraegen, 2000; Reavens, 2005; Hussein, Christen, Raji, Thomas, Frank & John, 2009). The relationship between insulin resistance and the changes in compensatory hyperinsulinemia and clinical syndrome include T2DM, cardiovascular diseases, essential hypertension, certain forms of cancer and sleep apnea (Yu, Chen & Cline, 1991; Paollisso & Howard, 1998; Reavens, 2005)

An estimated 30-50% of overweight youth exhibit the metabolic syndrome phenotype (Huang, *et al*; 2007), placing them at high risk for the premature development of cardiovascular disease and type 2 diabetes (Ford2005; McGill & McMahan, 2010). The core defect linking obesity to chronic disease risk is thought to be peripheral insulin resistance (Reaven & Banting, 1988). It has been observed that children with the metabolic syndrome are significantly more insulin resistant compared with those without the disorder even after controlling for adiposity (Cruz, Weigensberg, Huang, Bell,Shaibi, & Goran,2004)

Insulin resistance is defined as the inability of circulating insulin to exert a normal physiological effect at the target tissue classically described as impaired insulin stimulated skeletal muscle uptake (Shaibi, Robert & Goran, 2008). It is the decreased ability of peripheral target tissues to respond properly to normal concentration of insulin (Landiberg, 1986; Neel, Weder & Julius, 1998). Insulin resistance, an impaired biological response to circulating insulin, is a disorder common to range of metabolic diseases, including T2DM, glucose intolerance, obesity, dyslipidermia, hypertension and cardiovascular diseases (Reveans, 1988; Yu, Chen & Cline; 2002; Dullo, 2005).

Insulin resistance is a major feature of common metabolic dysfunction which is strongly associated with mitochondrial dysfunction, endoplasmic reticulum, stress and inflammation in the pathogenic of T2DM (Laakson & Sen 2000; Satyamarayena & Chakrapani, 2009). Insulin resistance is exacerbarated by aspects of modern Westernized lifestyle as overeating, sedentary and stressful life

(Goodyear & Smith, 1994). In order words, an insulin resistant individual has low insulin sensitivity, and an insulin sensitive person is not insulin resistant. The gold standard for determining insulin resistance in vivo is the hyperinsulinemic-euglycemic clamp technique (DeFronzol, Tobin & Andres, 1979).This technique provides for a direct measure of glucose uptake under insulin-stimulated conditions. Insulin is infused intravenously at predetermined supraphysiologic levels, whereas glucose is simultaneously infused at variable rate to maintain euglycemia. The rate at which glucose is infused under steady-state condition provides for a measure of insulin resistance with higher rates of glucose infusion equating to lower level of insulin resistance and vice versa (DeFronzol, *et al*; 1979).

When insulin-resistant individuals cannot maintain the degree of hyperinsulinemia needed to overcome the defect in insulin action, type 2 diabetes develops (Reavens, 1988). The combination of insulin resistance and compensatory hyperinsulinemia prevents the development of frank hyperglycemia, but greatly increases the risk of having some degree of glucose intolerance, a high plasma triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) concentration, and essential hypertension (Reavens, 1988). Individuals displaying this cluster of abnormalities associated with insulin-resistance/compensatory hyperinsulinemia were at significant increased risk of cardiovascular disease (CVD) (Reavens, 1988).

Disparate clinical implications of insulin resistance and its clinical consequences have broadened considerably, and the adverse clinical outcomes extend beyond T2DM and CVD. The insulin resistance syndrome (IRS) seems to provide a pathological construct with which to view the different abnormalities and clinical syndromes that occur more commonly in insulin-resistant individuals. Because there is no simple clinical way to quantify insulin resistance, the alternative is to either initiate similar effort at weight loss in all overweight/obese persons or to use surrogate estimation of insulin resistance to identify those who will benefit the most from weight loss. Health care professionals usually rely on measurement of fasting plasma insulin (FPI) concentration, or various formulae involving the use of both fasting plasma glucose (FPG) and insulin concentration (HOMA-IR-QUICK,FPGI x FPI.) to

indentify insulin resistant person. FPI concentrations are reasonably predictive of direct measurement of insulin resistance in nondiabetic individuals, but the relationship (r-value~ 0.6) only accounts for ~ 36% of the variability in insulin action (Reavens, 2005)

Insulin sensitivity improved when non-diabetic overweight/obese individuals lost weight, which was associated with a decrease in the plasma insulin response to oral glucose and lower plasma TG concentration (Olefsky, Farquhar & Reveans, 1974). Under hyperinsulinemia-euglycemic clamps in vivo, insulin-stimulated glucose utilization in animals is lower in skeletal muscle (by 20-43%), but higher in white adipose tissue (by two to threefold), thereby suggesting start of insulin resistance in skeletal muscles and insulin hyper responsiveness in white adipose tissue (Cettour-Rose, Same & Russell, 2005). Impaired translocation of GLUT-4 from intracellular stores to the plasma membrane is implicated in the decreased ability of insulin to stimulate glucose uptake. Aspects of the insulin signaling pathway responsible for GLUT-4 translocation including insulin receptor substrate (IRS), phosphorylation and phosphatidylinositol-3, Kinase (P13K) activity are reduced in insulin resistance skeletal muscle of type 2 diabetic patients (Goodyear, Giorgeno, Sherman, Carey, Smith & Dohm, 1995; Bjornholm, Kawann, Lehtihert & Zierath, 1997; Kim, Abbasi, Lamendola, Laughlin & Reveans, 2001; Fisher, Gao, Han, Holloszy & Nolte; 2008).

Evidence suggests that an oversupply of lipid can upsets the interaction between lipid and carbohydrate metabolism, necessary for maintenance of fuel homeostasis and may result in the condition of insulin resistance and its related disorders (Hegarty, Furler, Ye, Cooney & Kraegen, 2003). A primary role for elevated free fatty acid (FFA) availability in the development of muscle insulin resistance was first suggested by Randle, Garland, Hales & Newsholm, (1963), based on the observation that high plasma concentration of FFA is commonly associated with diabetes and other disorders of carbohydrate metabolism. To support this hypothesis, experiments demonstrated that insulin resistance can be induced within hours by lipid infusion (Feranmini, Barrett, Bevilaeyua & Fronzo, 1983; Bodden, Prince & Perseghin, 1996; Chatley, Hentirachchi, Chisholm & Kragan, 1998). Studies of a

number of genetic models of insulin resistance also implicated increased lipid availability in the pathogenesis of this disorder. Prevence, Landa & Zideck (2002) reported that transgenic expression of the fatty acid transport CD36/FAT in spontaneously hypertensive rats with genetic deficiency in CD36/FAT ameliorates their insulin resistance in association with reductions in circulating FFA.

The ability of insulin to stimulate muscle glucose uptake and inhibit free fatty acids (FFA) release from the adipose tissue is highly correlated (Abbasi, McLaughlin, Lamendola, Kim & Tanaka, 2000) and the similar degree of insulin resistance in these two tissues initiates the series of events that lead to the abnormalities and clinical syndromes. Increase in plasma insulin (muscles insulin resistance) and FFA (adipose tissue insulin resistance) concentration act upon a liver that is insulin sensitive to stimulate hepatic TG synthesis (Olesfsky et al; 1974; Reavens, Lerner, Stern & Farqular, 1967). One consequence of these events will be an increase in hepatic very-low-density lipoprotein (VLDL) – TG synthesis and secretion, leading to hypertriglyceridemia, while at the same time there will be a tendency for the fat content of the liver to increase and no alcoholic fatty liver disease to develop. In overweight/obese individuals, the plasma TG/HDL-C concentration is a good a surrogate marker of insulin resistance as is FPI concentration; it can be used to identify individuals who have the athreroganic profile that characterizes the IRS and thereby are at increased risk of CVD. It is suggested that overweight/obese person with a TG/HDL-C concentration ratio mg/dl ≥ 3.0 is highly likely to be both insulin resistant and at increased CVD risk; the higher the value, the less sensitive and the more specific ratio, whereas value < 3.0 increase sensitivity and lose specificity (McLaughlin, Abbasi, Cheal, Chu, Lamendola & Reveans, 2003).

Increased lipid availability may also increase the activity of the hexosamine pathway, a quantitatively small route of glucose metabolism that has been suggested to function as a nutrient sensing mechanism, but which has also been implicated in the development of insulin resistance (Rossertti, 2000, Bachman, Dahldo & Brechtol, 2001; Boden, Lebased, Schanzhomko & Lomieuri, 2001; Itani, Ruderman, Schmieder & Boden, 2002). Kim, Fulmore & Chen, (2000), reported that transgenic

mice that lack white adipose tissue (WAT) are surely insulin resistant and demonstrated a twofold increase in muscle triglyceride content.

Long-chain acetyl-COAs, (LCA COAs) are the activated form of intracellular FFA, produced by the action of ACOAs. LCA COAs content of skeletal muscle is increased in insulin-resistant humans (Ellis, Poynten & Lowy, 2000). Diacyglycerol (DAG) and protein kinase C, an intermediate of both triglyceride and phospholipids metabolism, has been shown to accumulate in the insulin-resistant muscle of high fat fed rats (Oakes, Kennedy, Jenkins, Laybutt, Chisholm & Kraegan, 1994; Schmitz-Peiffer, Browne & Oakes, 1997), as well as transgenic mice with muscle specific or expression of lipoprotein lipase (LPL) (Kim *et al;* 2001). In human, fatty acid induced muscle insulin resistance was recently found to be associated temporarily with increased DAG mass and with PKC isoform (membrane translocation) (Itani *et al*; 2002). A reduction in lipid availability and accumulation with the skeletal muscle is thought to be central to the insulin sensitization effects of the thiazolidineolione class of antidiabetic agents (Oakes et al; 1994).

2.3.4 Experimental Studies on the Effect of Exercise Training on Insulin, Insulin Sensitivity and Insulin Resistance.

Increased concentration of circulating insulin-like growth factor-1 (IGF-1) or IGF-1 relative to IGF-binding proteins (IGFBPs) are associated with increased risk of developing several forms of cancer. Conversely, exercise is linked with reduced risk. Nishida, Matsubara, Tobina, Shindo,Tokuyama & Tanaka, (2010), investigated the effect of a low-intensity exercise program on circulating levels of IGF-1, IGFBF-1, and IGFBP-3, in previously sedentary males; fourteen healthy men participated in cycle ergo meter training at lacerate threshold intensity for 60 min/day, 5 days/week for 6 weeks. After aerobic training, insulin sensitivity improved by 20%, while fasting insulin levels decreased by 13%. Simultaneously, low-intensity aerobic training decreased the circulating levels of IGF-1 by 9% while IGFBP-1 levels increased by 16%. An interesting finding was that higher retraining level of IGF-1 was

associated with greater decline in IGF-1 with training. Insulin-sensitizing low intensity aerobic exercise is thus considered to be an effective method for down regulating IGF-1 and unregulating of IGFBP-1 level.

Anderson, Polasnky, Bryden, Roginski, Patterson & Reamer, (1982) investigated the effect of exercise (running) on serum glucose, insulin, glucagon and chromium excretion. To test whether chromium is also associated with the exercise-induced increases in glucose utilization, urinary chromium excretion, serum glucose, insulin and glucagon of nine male runners (23-46 years) were evaluated. Blood samples were taken prior to immediately following and 2hr after a strenuous 6-mile run. Urine samples were also taken at these times, and total daily urine collections were made the day of the run and the following day. The results revealed that serum insulin levels were not altered significantly.

Wolfe, Nedet, Shaw, Stephenson & Wolfe, (1986) evaluated the role of changes in insulin and glucagon in glucose homeostasis in exercise. The experiment was performed to determine if plasma glucose homeostasis is maintained in normal human volunteers during light exercise (40% maximal oxygen consumption [$Vo_{2\ max}$]) when changes in insulin and glucagon are prevented. Hormonal control was achieved by the infusion of somatostatin, insulin, and glucagon. Glucose kinetics and oxidation rates were determined with stable isotopic tracers of glucose, and by indirect calorimetry. Two different rates of replacements of insulin and glucagon were used; in one group, insulin was clamped at 19.8$\pm$, 2.6µu/ml (high-insulin group), and in the other group, insulin was clamped at 9.2$\pm$1.3 µu/ml (low -insulin group). Glucagon was maintained at 261$\pm$16.2 and 124$\pm$6.4 pg/ml, respectively, in the high-insulin and low-insulin groups. The results indicated that when hormones were not infused, insulin concentration decreased slightly during exercise, with lower values at 45 and 60 minutes of exercise than in the basal period ($P<0.05$). With hormonal control, no significant changes in insulin occurred through the entire experimental protocol. In the high-insulin; group, the insulin level was constant at ~20µu/ml and in the low-insulin group, insulin values were ~9µu/ml. In the control subjects, the average insulin concentration was 11.1$\pm$ 2.0 µm/ml. It was concluded that during light exercise there

must be a reduction in insulin concentration if plasma glucose homeostasis is to be maintained in the Low-insulin groups. Findings indicate that glucagon concentration appeared to increase slightly in exercise, but the change was not statistically significant. With hormonal control, no significant changes in insulin or glucagon occurred throughout the entire experimental protocol. In the high-insulin group, glucagon remained ~260pg/ml. The insulin and glucagon values in the low insulin group were ~9μu/ml and 130pg/ml respectively. In the control subject, the glucagon concentration was 141±16.8 pg/ml. They concluded that during light exercise, there must be a reduction in insulin concentration and/or an increase in glucagon concentration if plasma glucose homeostasis is to be maintained. If such changes do not occur, hypoglycemia and exhaustion may occur.

Khoo *et al*; (2010) studied the effect of exenatide on circulating glucose, insulin, glucagon, cortisol and catecholamines in healthy volunteers during exercise. The hypothesis was that exenatide, a glucagon like peptide-1 agonist, is a treatment for type 2 diabetes mellitus that stimulates insulin and suppresses glucagon

2.3.4a Experimental Studies on the Effect of Exercise Training on Insulin Sensitivity

Few studies have evaluated the effect of aerobic physical training on insulin sensitivity in subjects with type 2 diabetes treated with oral hypoglycermic agents. Most studies that involved non obese subjects showed enhanced insulin sensitivity, whereas studies involving obese subjects with type 2 diabetes are inconsistent because of concomitant fat loss. It is in view of this that Tansey *et al*; (2006) studied the effect of moderate aerobic exercise training on insulin sensitivity in type 2 diabetic men with oral hypoglycermic agents, and wanted to know if insulin sensitivity is enhanced only in non obese subjects. They used thirteen men with type 2 diabetes (6 non obese and 7 obese) treated with oral hypoglycermic agents carried out 12 week ergocycle program at 60% Vo2 max, one hour thrice a week. Diet and medication were maintained throughout the study. Insulin sensitivity was assessed with the euglycemic clamp technique. The results indicated that Vo_2 peak (ml/kg/m) increased with exercise training. There were no significant changes in fat mass, percent body fat, fasting plasma glucose and

insulin levels, glycated hemoglobin levels, or insulin sensitivity. However, when the subjects were separated into two groups, they showed different insulin sensitivity adaptation to training. In fact, non obese subjects with type 2 diabetes showed an increase in insulin sensitivity, whereas no change was observed in the obese subjects. These findings suggest that moderate aerobic exercise training of 3 months duration enhanced insulin sensitivity only in non obese men with type 2 diabetes. Obese men with type 2 diabetes showed no benefit. The adiposity per se may be a determining factor in the exercise induced metabolic benefit of exercise training in subjects with type 2 diabetes.

A growing body of literature suggests that children who participate in regular physical activity may have higher insulin sensitivity levels compared with their more sedentary counterparts (Kelly & Goodpaster, 2011). However, most of the work has used self reported estimates of physical activity that are prone to reporting errors. Furthermore, whether activity is protective against insulin resistance, independent of body composition or obesity is a matter of debate. Bunt, Salbe, Harpe, Hanson & Tataranni, (2003) attempted to shed more light on this question by examining the cross-sectional associations and prospective relations between physical activity and insulin sensitivity in Pima Indian children at high risk for developing type 2diabetes. They found that both physical activity behavior (measured via questionnaire) and physical activity level (measured via doubly labeled water) were significantly and directly related to insulin sensitivity. Although these associations hold true after adjusting for sex ($r = 0.24$; $P = 0.02$ and $r = 0.21$; $P = 0.02$ respectively) when measures of body composition were controlled for a multiple regression analysis.

Physical activity (by either measure, was no longer a significant independent determinant of insulin sensitivity ($P = 0.014$; $P = 0.006$ and $P = 0.059$; $P = 0.69$, respectively). When the authors analyzed their data over 5 year period, they found that both activity and insulin sensitivity significantly decreased in their cohort but noted that youth with the smallest decrease in physical activity behavior exhibited the smallest decrements in insulin resistance independent of body mass changes ($r = 0.22$; $P = 0.04$ for change in insulin sensitivity and activity behavior). These results suggested that youth who

maintained an active lifestyle over a time were somewhat protected from the adipose-related development of insulin resistance.

Landt *et al;* (1985) investigated the influence of a program of exercise training consisting of three weekly sessions, each 45 min long, for 12 wk, on indices of physical fitness, glycemic control, and insulin sensitivity in nine adolescents with type 1 diabetes. Six age-matched adolescents with diabetes of equivalent duration served as non-exercised controls. All subjects were instructed not to change daily insulin dose or caloric intake. In the exercised group, maximal oxygen uptake during graded cycle ergometry to volitional exhaustion increased by 9 $\pm$ 2.7% ($P< 0.01$) and lean body mass increased by 4 $\pm$ 1.8% ($P<0.05$). Insulin sensitivity, assessed via the euglycemic clamp technique at insulin infusion rates of mU/M2/min, showed an increased in insulin sensitivity of 23 $\pm$ 5% ($P< 0.01$). None of these indices changed in the control group, despite increased insulin sensitivity, glycohemoglobin levels remain at 12 $\pm$ 1% before and after the 12 week of exercise training, indicating no improvement in overall glycemic control. No increase in hypoglycemic reactions was reported in either group. They concluded that exercise training may be a valuable adjunct in managing type 1diabetes providing there is concomitant attention to diet and insulin. Exercise training alone, however, does not improve glycemic control, although it improves physical fitness and insulin resistance.

Data are limited on the effects of controlled aerobic exercise program (with weight loss) on insulin sensitivity and glucose metabolism in children and adolescents. As a result, Van der Heijden *et al*; (2009) study aimed at determining whether a controlled aerobic exercise program (without weight loss) improves peripheral and hepatic insulin sensitivity and affects glucose production (GPR), gluconeogenesis and glycogenolysis in sedentary lean and obese Hispanic adolescents. Twenty-nine post pubertal adolescents (14 lean: 15.1 $\pm$ 0.3 years 20.6 $\pm$0.8kg/m2, 18.9 $\pm$ 1.5% body fat and 15 obese: 15.6 $\pm$ 0.4%; 33.2 $\pm$ 0.9kg/m2, 38.4 $\pm$ 1.4% body fat (mean $\pm$ SE), completed in a 12 wk aerobic exercise program (4 x 30 min/week at > 70% of Vo2 peak). Peripheral and hepatic insulin sensitivity and glucose kinetics were quantified using GCMS pre- and post- exercise. The results showed that no weight loss

occurred. Lean and obese participants complied well with the program (~90% of the exercise sessions attended, resulting in -15% increases in fitness in both groups). Peripheral and hepatic insulin sensitivity were higher in lean than obese adolescents but increased in both groups, peripheral insulin sensitivity by 35 $\pm$ 14% (lean) ($P < 0.05$) and 59 $\pm$ 19% (obese) ($P < 0.01$) and hepatic insulin sensitivity by 19 $\pm$ 7% (lean) ($P < 0.05$) and 23 $\pm$ 4% (obese) ($P < 0.01$). GPR, gluconeogensis and glycogenolysis did not differ between the groups. GPR decreases slightly, 3$\pm$1% (lean) ($P < 0.05$), and 4 $\pm$ 1% (obese) (< 0.01). Gluconeogensis remained unchanged, while glycogenolysis decreased in the obese group ($P < 0.01$). They concluded that this well accepted aerobic exercise program without weight loss is a promising strategy to improve peripheral and hepatic insulin sensitivity in lean and obese sedentary adolescents.

Similarly, Koo, Han, Ahn, Jing, Kim & Min, (2010) examined the effects of physical activity with or without dietary restriction for 3 months on regional fat and insulin sensitivity and compared the effect of total energy expenditure from all levels of physical activity with that of physical activity energy expenditure from moderate-to-vigorous exercise in obese women with type 2 diabetes. In this randomized controlled trial, they assessed change of body weight, abdominal visceral fat area, subcutaneous fat area and insulin sensitivity, expressed as K_{rTT}. and monitored total energy expenditure and physical activity energy expenditure using an accelerometer during a 12 week intervention in four groups, control, diet, exercise and diet plus exercise. The results indicated that the mean body mass index (BMI) was 28.0 $\pm$ 2.7 kg/m2 and the mean duration of diabetes was 8 $\pm$ 6 years. Both the diet and diet plus exercise groups showed significant body weight loss compared with the control group ($P < 0.05$). However, the visceral fat area was reduced only in the diet and exercise group (P – 0.017) and the subcutaneous fat area (P – 0.020) and mean total energy expenditure was an independent determinant of visceral fat area ($P = 0.002$). Insulin sensitivity K_{rTT} was associated with physical activity energy expenditure ($P = 0.006$), energy intake ($P = 0.047$) and the change in fructosamine level (P – 0.016) but not with change in body weight, subcutaneous fat area, visceral fat area or adipoline level. They concluded that exercise had an additive effect to dietary restriction on visceral fat reduction.

Visceral fat area was associated with total energy expenditure, but insulin sensitivity was associated with physical activity energy expenditure.

Obesity is characterized by excessive rates of plasma fatty acid mobilization and uptake, which play a key role in mediating insulin resistance. While weight loss via diet-only or a diet - exercise program clearing improves insulin sensitivity, the precise mechanism modulating this improvement are not completely understood,. It is in light of the above that Schenk, Harber, Shrivastava, Burrant & Horowitz, (2009), in their study investigated "improved insulin sensitivity after weight loss and exercise training is mediated by a reduction in plasma fatty acid mobilization, not enhanced oxidative capacity''. The purpose of the study was to determine the role of the reduced fatty acid mobilization and uptake after weight loss in obese women who were randomly assigned to lifestyle interventions of either weight loss without exercise (WT) (n=7) or weight loss - exercise program (WL $\pm$ Ex) (N=10). Before and after losing 12% of their body weight, they measured insulin sensitivity (SI), systemic fatty acid rate of appearance (Ra) and disappearance (Rd), oxidative capacity, and markers for prior-inflammatory pathways in skeletal muscles. Fatty acid Ra and Rd were reduced by ~30% after both interventions ($P < 0.05$). While oxidative capacity increased 25% in Wt $\pm$ Ex (compared with no increase after WT), the improvement in SI was identical in both groups (~60%, $P < 0.05$), and skeletal muscle pro-inflammatory pathways were reduced ($P < 0.05$). Similarly in both groups when they artificially increased fatty acid mobilization after weight loss to pre-weight-loss levels via an overnight lipid infusion, the improvement in S1 was almost completely reversed. Importantly, WL - Ex did not protect against Lipid – induced reversal in S1 despite a significant increase in resting whole-body fat oxidation and a marked increased in skeletal muscle oxidative capacity.

In conclusion, reduced fatty acid mobilization and uptake appears to be a primary mediator of improved insulin sensitivity after weight loss.

2.3.4b Experimental Studies on the Effect of Exercise Training on Insulin Resistance

The metabolic syndrome (Ms) is a cluster of risk factors such as elevated blood pressure, dyslipidemia, and central obesity, associated with various biological manifestations, including hyperglycermia and insulin resistance (Despress, 1994; Boden et al; 1996; Reavens, 2003). Patients with the MS have an increased risk for cardiovascular morbidity and mortality. The goal standard for determining insulin resistance in vivo is the hyperinsulinemic-euglycemic clamp technique. This technique provides for a direct measure of glucose uptake under insulin-stimulated conditions. Briefly, insulin is infused intravenously at predetermined supraphysiologic levels, whereas glucose is simultaneously infused at a variable rate to maintain euglycemia. The rate at which glucose is infused under steady-state condition provides for a measure of insulin resistance with higher rates of glucose-infusion equating to lower levels of insulin resistance and vice-versa (Defrozo, Tobin & Andres, 1979).

In one of the largest cross-sectional studies to date to examine the association between objectively measured physical activity and insulin resistance in youth, Anderson *et al*; (2006) used accelemetry to objectively quantify moderate-to-vigorous physical activity in 1832 European children aged 9 and 15 years. They found a weak association ($r - 0.17$; $P<0.001$) between physical activity and insulin resistance.

Several promising studies in a variety of population and setting have demonstrated that exercise training can be a potent intervention strategy for improving insulin resistance in overweight youth (Hussein et al; 2009). Ferguson, Gutin, Le, Karp, Litaker, Humpries, Okuyama, Riggs & Owen, (1999), recruited 79 overweight African American and white youths, aged 7-11 years who were randomized to either receive 4 months of exercise training or are included for 4 months on a non-exercise waiting list. The program was offered 5 d-wk1, and youth were encouraged (via incentives) to maintain a heart rate above 150 beats min^{-1} throughout the semi-structured aerobic exercise session. It was found that youth randomized to the exercise group exhibited a 10% decrease in fasting insulin concentrations as a result of the program compared, with a negligible increase in the control group. The decrease in fasting insulin was not accompanied by a change in fasting glucose and was interpreted to

suggest an improvement in insulin sensitivity in trained youth. Ferguson *et al*, (1999), used a cross-over design, whereby the trained youth were subsequently followed for an additional 4 months after the program to examine the sustainability of the improvements. Not surprisingly, they found that 4 months of detraining resulted in a reversal of the exercise effects, suggesting that exercise patterns must be continued to maintain improvement.

In a related follow-up study, Kang, Gutin,Barbeau, Owens, Lemmon, Allison, Litaker & Le, (2002), examined whether comparable exercise induced improvement in fasting insulin could be observed in 13 to 16 year old overweight adolescents who performed exercise for 8 months. In contrast to the findings, Kang *et al*; (2002) did not observe similar improvements in insulin resistance in the adolescents. Although the programs were not comparable in terms of length, the latter being 8 months and the former being 4 months, the lack of an exercise effect probably had more to do with differences in a study population than program duration.

Other studies have established that adolescents can significantly improve insulin resistance in response to exercise training. Nassis *et al*; (2005), examined the effects of 12 wk of aerobic exercise training on insulin response to an oral glucose challenge in overweight adolescent girls. The program consisted of three- 40 min supervised sessions per week at moderate exercise intensity (heart rate > 150 beat min^{-1}). Compared with baseline values, the girls exhibited a decrease in serum insulin concentrations in response to a 2 hr oral glucose tolerance test. Collectively, the lower insulin concentrations resulted in 24% reduction in insulin area under the curve ($P < 0.05$), an indication of improved whole body insulin sensitivity. This improvement in insulin sensitivity was not accompanied by changes in body mass or body fat percentage which suggested an independent effect of exercise on insulin metabolism.

Similarly Shaibi *et al*; (2006), examined the effects of a 16-wk resistance training intervention on directly measured insulin sensitivity (FS1VGTT) in overweight adolescent boys at high risk for developing type 2 diabetes. Youth were randomized either to a twice per week progressive exercise program or a

non-exercising wait-list control group. The exercise sessions were delivered at a local community center and were monitored closely by research personnel trainers. Each session consisted of single and multipoint exercise for approximately 1hr. Training volume was increased at presented intervals. Within the program, loads were adjusted within a structured protocol. It was discovered that exercise group increase insulin sensitivity 45% over baseline values compared with a change in the control youth. Although large variability in the individual response to exercise training was observed, 90% of participants exhibited an increase in insulin sensitivity.

Imperatore, Cheng, Williams, Fulton & Gregg, (2006), examined the relationship between physical activities (by questionnaire) and insulin sensitivity in a representative sample of 1783 adolescents. After controlling for age, ethnicity, and BMI; a weak positive association between activity and insulin sensitivity was found ($r - 0.11$; $P < 0.001$). When data were examined separately by sex, this relationship remained significant only for boys. They concluded that in girls, a physically active lifestyle is not significantly associated with insulin sensitively but rather may impact insulin metabolism indirectly through effects on adiposity in contrast to boys where a direct and independent effect on insulin sensitivity remained.

A growing body of evidence supports the notion that overweight youth who participate in a structured exercise program can significantly improve insulin resistance. These proofs of concept studies are scientifically important for establishing the efficacy of exercise to improve insulin resistance and decrease diabetes risk. In parallel with the pediatric obesity epidemic, the incidence of impaired glucose tolerance and type 2diabetes has increased among youth. Insulin resistance is thought to be central to the patho-physiology of these obesity-related disorders. A growing body of literature suggested that exercise may ameliorate insulin resistance and thus partially reduce the long-term diabetes risk in overweight youth.

2.4 The Role of Glucagon in Cabohydrate Metabolism

Glucagon, secreted from alpha cells or α cell in islet of Langerhan of Pancreas, is polypeptide with a molecular weight of 34, and contains 27 amino acids. Glucagon is synthesized from the preprohormonal precursor called preproglucagon in the cells of islet (Galbo et al; 1977;Godwin, 2010). In carbohydrate metabolism, about 32% of glucagon is degraded in liver and 20% in kidney. The cleaved glucagon fragments are excreted through urine (Sembuligan and Sembuligan 2010). Secretion of glucagon is inhibited by α-cells when glucose concentration is higher. Also, higher concentration of amino acids seems to increase glucagon secretion, while highly correlating free fatty acids (FFAs) seem to inhibit its release (Greenspan & Gardner, 2004). The primary regulator of plasma glucagon is the circulating glucose (Dunning, Foley & Ahren, 2005). A drop to 3.7 mmol/l (-67mg/dl) in plasma glucose is potent stimulus for glucagon secretion from the alpha cells of the pancreas (Mitrakou, Ryan, Veneman, Mokan, Jensen, Kiss, Durrant, Cryer & Gerich, 1991; Cryer, 2001). Glucagon binds its G-protein-coupled receptor at the liver. This initiates a stimulating cascade via increasing adenylcyclase actively and increase cyclic adenosine monophosphate (CAMP) (Lavoie, 2005). Cyclic adenosine monophosphate phosphorylates several intracellular proteins, which leads to phosphorylation of glycogen phosphorylase to its more active “a” form. This active form induces rapid glycogenolysis. Simultaneously, glucagon binding at the liver also stimulates gluconeogenic activity by phosphorylating the fructose 26 biphosphatose/phosphofructokinase-2 enzymes, activating its phosphatase activity to decrease the F26BP in the cell (Roder *et al*; 2001). Increases in plasma amino acids stimulate glucagon production; the presence of high amino acid levels can then be utilized in gluconeogenesis at the liver (Dunning *et al*; 2005). The primary role of glucagon is to mobilize fuel (Plowman & Smith, 2008).

Actions of glucagon are antagonistic to those of insulin. It increases the blood sugar level, increases the peripheral utilization of lipids and facilitates the conversion of protein into glucose (Koivisto, Soman, Nadel, Tamborlane & Felig, 1980; Mitrakou et al; 1991; Calbat & Maclean, 2002; Greenspan & Gardner, 2004).

On carbohydrate metabolism, glucagon increases glucogenolysis in liver and does not induce glycogenolysis in muscles (Brouns & Cargill, 2002). It increases gluconeogenesis in liver by activating the enzymes which convert pyruviate into phospharnol pyruviate. It increases the transport of amino acids into liver cells for glucose formation. Likewise in protein metabolism, glucagon increases transport of amino acids into liver cells, which are utilized for gluconeogenesis (Landry, 2002; Rorsman, 2005).

Glucagon shows lipolytic and ketogenic action on fat metabolism. It increases lipolysis by increasing the release of free fatty acids from adipose tissues and making them available for peripheral utilization. The lipolytic activity of glucagon in turn promotes ketogenesis (formation of ketone bodies) in liver. Glucagon inhibits the secretion of gastric juice and increases secretion of bile in liver. A decrease in blood glucose level below 80mg/dl of blood, α cell of islet of langerhan is stimulated and more glucagon is released. On the other hand, when blood sugar level is elevated, α cell is inhibited and the secretion of glucagon decreases (, Landry 2002; Williams, 2007).Those factors that inhibit glucagon secretion are somatostatin (inhibits secretion of both insulin and glucagon), insulin, FFA and ketones (Waugh &Grant 2006; Sambuligan & Sembulingan, 2010).

2.4.1 Effect of Exercise Training on Glucagon

With increased exercise duration, the amount of cortisol secreted increases in order to preserve plasma glucose with a resultant increase in glucagon to promote gluconeogenesis.. These signals interact in a coordinated fashion (Dunning et al; 2005), to control glucagon secretion from alpha cells of the pancreas. During prolonged exercise, the main stimulus that promotes an increase in glucagon secretion from the pancreas alpha cells is a drop in plasma glucose and concomitant drop in plasma insulin. It has been further noted that a fall in insulin in exercising dogs increases the sensitivity of the liver to glucagon outside of any glucagon changes (Zinker *et al*; 1994), perhaps due to increased receptor number, as exhibited by Legare, Drouin, Milot, Massiocotte, Peronnet,Massiocotte & Lavoie, (2001), with endurance trained rats. Studies in human suggested that epinephrine (E) fluctuation may

attenuate plasma glucose changes in the face of clamped glucagon or insulin levels (Tuttle, Marker, Dalsky, Schwaartz, Shab, Clutter, Holloszy & Cryer, 1998, Greenspan & Gardner, 2006).

Exercise is reported to be a unique model for studying glucagon action, because it allows for an increment in glucagon to be studied without creating hyperglycemia or hyperinsulinemia, both of which may influence glutamine metabolism (Abumrad, Williams, Frexes-Steed, Geer, Flakoll, Cersosimo, Brown, Melko, Bulus, Hourani, Hubbard & Glrushan, 1989). The absence of these two factors that suppress hepatic glucagon action allows the full effect of an increment in glucagon to be assessed. In normal people, during acute exercise of moderate duration, blood glucose remains constant as a result of hormonal adaptation that insure increased hepatic glucose utilization rate of exercising muscle (Landt *et al*; 1985). Glucose uptake by exercising muscles is increased 7 to 20 fold above basal levels, and to meet this increased need for glucose, hepatic glucose production is increased three to five fold (Wahren, Felig, Ahlbourg & Jorfeldt 1971; Bowen, 1999; Calbat & Maclean, 2002) and plasma glucagon increased while serum insulin decreased (Purett, 1970, Calbat & Maclean, 2002; Sato et al; 2003). Krishna *et al*; (2013) reported a twofold rise in glucagon concentration and fall in plasma insulin in their study to determine the role of glucagon in hepatic glutamine metabolism during exercise. The accelerated glucose uptake rate during exercise is compensated for by enhanced hepatic glucose production; hence, normoglycemic level is maintained throughout the course of physical activity (Endocrine Web, 1998; Ganong, 2001; Roy & Parker, 2007). Insulin and glucagon are implicated in the tissue metabolism of blood levels of glucose, fatty acids, triglycerides and amino acids (Kang et al; 1996; Ganong, 2001; 2011). Modern medical treatment of diabetes is based on the understanding of the mechanism involved in the regulation of these hormones. A fall in blood glucose below 4mmol/l leads to a significant decrease in insulin secretion and delivery of glucagon to the blood by alpha cells of the pancreas (Bowen,1999; Achten & Jeukendrup, 2004; Guyton & Hall 2006).The simultaneous secretion of

insulin and glucagon by the respective cells controls glucose metabolism (Slentz, Tenner, Bateman, Durheim, Huffman,Houmand & Kraus, 2009). Increase in insulin levels inhibits glucagon release from alpha cells, thus, controlling the glucagon's activation of hepatic gluconeogenesis and lipolysis in adipose tissues (Calbat & Maclean, 2002). On the other hand, glucagon secretion increases with the decrease in blood sugar levels, countering the effects of insulin on glucagon and fat metabolism (Rorsman, 2005).

During aerobic exercise, the serum insulin concentration normally falls with a rise in plasma glucagon. Khoo *et al*; (2010) in their study, reported that insulin/glucagon molar ratio rose with exenatide at rest (P<.01), then fall during exercise with placebo and with exenatide (exernatide is a glucagon like peptide-1 agonist, is a treatment for type 2 diabetes mellitus that stimulates insulin and suppresses glucagon secretion in a glucose dependent manner). Landry (2002) reported that blood levels of insulin begin to decrease about 10 minutes into aerobic exercise and continue to decrease through about 70 minutes of exercise. In like manner, glucagon is also reported to typically begin to be secreted beyond 30 minutes of exercise when blood glucose levels may begin to decrease (Galbo, 1983; Bent, 1986; Bowen, 1999).With plasma insulin decrease with long- term exercise, it should be no surprise that the plasma glucagon concentration increases (Gyntelberg, Rennie, Hickson & Holloszy, 1977, Bent, 1986; Ganong, 2001). This increase in plasma glucagon favors the mobilization of FFA from adipose tissue and glucose from the liver, as well as an increase in gluconeogenesis. Overall, the reciprocal response of insulin and glucagon favors the maintenance of the plasma glucose concentration at a time when the muscle is using plasma glucose at a high rate. Following an endurance training program, glucagon response to a fix exercise task is diminished to the point that there is no increase during exercise. In effect, endurance training allows the plasma glucose concentration to be maintained with little or no changes in insulin and glucagon. This is related in part to an increase in glucagon sensitivity in the liver (Laycock & Wise, 1983; Drouin, Lavoie, Bourque, Durcos, Passion & Chiassion,

1998; Achten & Jeukendrup, 2004), a decrease in glucose uptake by muscle (Richter, Mikines, Galbo & Kliens, 1989, Fisher et al; 2008), and an increase in the muscle use of fat as fuel.

Studies have shown that insulin/glucagon molar ratio rose with exenatitude at rest and fell during exercise. Krishna *et al*; (2013), reported that plasma glucagon concentration rose two-fold on the course of the exercise period. The exercise induced increment in glucagon resulted in gradual increase in hepatic fractional glutamine excretion that reached sevenfold basal by the end of exercise period.

2.4.2 Experimental Studies on the Effect of Exercise Training on Glucagon

Glucagon response to exercise is critical for accelerated hepatic glutamine metabolism and nitrogen disposal. Krishina *et al*; (2013), conducted a study to determine the role of glucagon in hepatic glutamine (Gln) metabolism during exercise. Sampling and infusion were implanted in anesthetized dogs. At least 16 days after surgery, an experiment consisting of a 120-minutes equilibrium period, a 30 min basal sampling period, and a 150 min exercise period, was performed in these animals. 5-15 Gln was infused throughout the experiment to measure GUT and liver Gln kinetics on the incorporation of Gln amide nitrogen into urea. Somatostatin was infused throughout the study; Glucagon was infused at a basal rate until the beginning of exercise. When the rate was gradually increased to stimulate the glucagon response to exercise, (n – 5 or 2) unchanged to maintain basal glucagon (n – 5). Insulin was infused during the equilibration and basal periods at rates designed to achieve stable euglycemia. The insulin infusion was reduced in both protocols to stimulate the exercise induced insulin decrement. Plasma glucagon concentration rose by two-fold over the course of the exercise period in SimG whereas concentrations were unchanged from basal in BasG. Concentration in BasG were significantly less than concentration in SimG from 75 to 150min ($P<0.01 – 0.01$). Plasma insulin fell similarly in SimG and BasG. Basal arterial glucose concentration were 109$\pm$ 62g 109$\pm$ 6 (mg/d/ in SinG, and BasG, respectively. Arterial Gln fell gradually when the glucagon response was stimulated ($P< 0.005$ at 75-100 min and 125-150 min) but was unchanged from basal when the glucagon response was maintained at basal. The exercise-induced increment in glucagon resulted in a gradual increase in hepatic fractional GLn

extraction that reached sevenfold basal by the end of the exercise period. These data show by use of the physiological perturbation of exercise, that glucagon is a physiological regulator of hepatic Gln metabolism in vivo.

Wolf *et al;* (1986), experiment was performed to determine if plasma glucose homeostasis is maintained in normal human volunteers during high exercise (40% $Vo_{2\ max}$) when changes in insulin and glucagon are prevented. Glucose kinetics and oxidation rates were determined with stable isotopic tracers of glucose, and by indirect calorimeter. Two different rates of replacement of insulin and glucagon were used. Glucagon was maintained at 261$\pm$ 16.2 and 124 $\pm$ 6.4 pg/ml respectively in the high-insulin and low-insulin. Anderson *et al;* (1982) investigated the effect of exercise (running) on serum glucose, insulin, glucagon and chromium excretion. To test whether chromium is also associated in glucose utilization, urinary chromium excretion, serum glucose, insulin and glucagon of nine male runners (23-46 years) were evaluated. Blood samples were taken prior to, immediately following, and 2 hours after a strenuous 6-mile run. Results indicated that mean serum glucagon immediately after running was significantly elevated compared with that observed prior to or 2 hour after running.

In their study on the effects of exenatide on circulating glucose, insulin, glucagon, cortisol and catecholamines in healthy volunteers during exercise, Khoo *et al*; (2010), studied eight non-diabetic men, who were 25.3 +/- 6.3 years of age with BMI of 24.7 $\pm$ 1.7 kg/m^2 (mean $\pm$ SD), using a randomized, crossover, double-blind investigation. After an overnight fast, participants received micro of subcutaneous exenatide or placebo and rested for 105 min before cycling at 60% of the Vo_2 max for 75 min and then recovering for a further 60 min. Findings indicated that insulin/glucagon molar ratio rose with exenatide at rest ($P<0.01$), then fell during exercise with placebo and with exenatide.

2.5 The Role of Lipids in Carbohydrate Metabolism

A special cause of reduced insulin action in skeletal muscle remains unknown, although aberrant lipid metabolism, and in particular an increased availability of lipid is strongly implicated (Ass,

2001; Hegarty *et al*; 2003). Triglyceride is true or natural fat composed of fatty acid and glycerol. Triglyceride is another fat in body serum. High level of triglycerides is also linked to heart disease. Many people who have heart diseases or diabetes have high triglyceride level (Wildman & Miller, 2004; Williams, 2007).Triglycerides, being a byproduct of carbohydrate metabolism, is transported in plasma mostly in the form of chylomicrons and very low density lipoprotein (VLDL), but are also present in low density lipoprotein (LDL) and high density lipoprotein (HDL) in small amount (Ochei & Okolhalkar, 2007; Sembuligan & Sembulingan, 2010).

Evidence suggests that an oversupply of lipid (hyperlipidemia) can upset the interaction between lipid and carbohydrate metabolism necessary for fuel homeostasis which may result in the condition of insulin resistance and its related disorders(Hegarty, Cooney, Kraegan & Furler, 2002; Dulloo, 2005).Based on the observation that free fatty acid (FFA)availability in the development of muscle insulin resistance , FFA is commonly associated with diabetes and other disorders of carbohydrate metabolism, (Chalkley *et al*; 1998; Roden 2000; Hegarty *et al*; 2003; Dulloo, 2005).TG optimal level < 150; borderline =200; high risk level< 200 mg/dl (Heyward, 1997

Studies of a number of genetic models of insulin resistance also implicate increased lipid availability in the pathogenesis of the disorder of diabetes. Increased lipid availability may also increase the activity of the hexosamine pathway, a quantitatively small route of glucose metabolism that has been suggested to function as a nutrient-sensing mechanism, but which has also been implicated into the development of insulin resistance (Rossetti, 2000). Serum level of cholesterol and triglycerides have for sometimes been implicated in or associated with the incidence of coronary heart diseases. Cholesterol plays a major role in human heart health. Triglyceride is linked to heart disease. Many people who have heart disease or diabetes have high triglyceride level (Peirce, 1999; McGill McMahan, 2010;). Lipids and lipoproteins abnormalities are prevalent in diabetic patients, as insulin deficiency and insulin resistance affect key enzymes and pathways in lipid metabolism (Feranmini et al; 1983; Paterson, Pattigrew, Dominizak & Small, 1991; Paollisso & Howard, 1998; Hegarty et al; 2002). Consequently, it is

not surprising that the risk of artherosclerotic coronary heart disease is higher in diabetics compared to non diabetic subjects (Kelley, Mokan, Simonean & Manderino, 1993; El-Hazmic & Warsy 1994; Hegarty *et al*; 2003; Wildman and Miller 2004; Ochei & Okolhalkar 2007).

Intramuscular lipid accumulation is now evident in a wide array of experimental models including insulin resistance induced acutely by lipid infusion in both humans (Bachmann et al; 2001; Boden et al; 2001; Itani et al; 2002), and rodents (Chakley et al; 1998; Griffin, Marculli & Cline, 1999; Yu et al; 2002). Kim, Mikoulina, Giaraldi, Hurry & Kahn, (2000b) reported that transgenic mice that lack white adipose tissue (WAT) are severely insulin resistant and demonstrate twofold increase muscle triglyceride content. The relevance of intramuscular lipid accumulation to the pathogenesis of fatty-acid induced insulin resistance is strengthened by the fact that it is associated with insulin resistance even in the absence of elevated plasma FFA levels.

In consonance with the foregoing, Anaja, Isah, Abdu, Aguye & Oboru, (1995), in a study of lipid profiles in diabetic Nigerians, examined levels of total cholesterol, triglycerides, high density lipoproteins, low density lipoprotein and atherogenic index of 30 fasting insulin dependent and 12 non-insulin dependent diabetics, as well as 50 healthy control subjects. It was observed that total blood cholesterol and triglyceride levels were significantly higher in diabetic patients than in control. They concluded that prevalence of lipid abnormalities in diabetic Nigerians is higher. In his study of the effects of aerobic exercise training on selected physiological variables in non- insulin dependent diabetics, Muhammad, (2003), in like manner identified the physiological variables that were in relationship to diabetes to include blood sugar, low density lipoprotein (LDL), triglycerides, total cholesterol and high density lipoprotein-cholesterol (HDL-C). Many components of metabolic syndrome are associated with a sedentary lifestyle include overweight, increased adipose tissue, HDL-C, and a trend towards increased triglycerides, blood pressure and glucose (Habibzadeh, 2010)

2.5.1 Effect of Exercise on Triglycerides

Physical inactivity or lack of exercise has been identified as one of the primary risk factors associated with increased incidence of arteriosclerosis and cardiovascular diseases. Researchers have found out that physically trained individual, activity of several enzymes, such as hepatic lipase and protein lipase are modified in such a way as to promote a more rapid catabolism of triglyceride and a greater production of HDL (Wildman &Miller 2004; Williams 2007). Many types of exercise appear to positively influence blood lipid profile. Such changes in lipid profiles related to exercise training include reduction in TG levels (Leon & Sanchez 2001; Durstine, Peter, Paul, Michael & DuBose, 2002; Schenk & Horowtz, 2007).

Several studies have reported the beneficial role of exercise training on triglyceride. Guo, Kawano, Piao, Itoh, Node & Sato, (2011), reported a significant improvement in triglycerides at the end of the three months aerobic exercise training on lipid profiles in Japanese workers. Kelley, Kelley & Vu Tran, (2005), reported a statistically significant improvement in triglycerides (x +_s.e.m.-16 +_ 7.3 mg/dl) due to effects of aerobic exercise on lipid and lipoprotein in overweight and obese adults. Tolfrey, Jones & Campbell, (2000), reported that trained or active children and adolescents demonstrate favorable levels of triglycerides. Habibzadeh (2010), reported that TC, TG and FBS significantly decreased (p 0.05) in a 2 month walking exercise in young obese women. Ahn, (2007), reported that one hour moderate intensity walking exercise, 5 days per week for 3 months, had no significant difference on body composition, TC and TG in obese post-menopausal women. In another study to assess the effects of aerobic exercise on selected physiological variables on non-insulin dependent diabetics, Muhammad (2003), observed a decrease in lipids and lipoprotein with the exception of HDL-C that showed an increase after 12 weeks of bench- step exercise training. Durstine, Grouse & Moffatt, (2001) in a meta-analysis of well controlled study, indicated that exercise volume of 1200-2200 calories per week is often effective at elevating HDL-C levels from 2-8 mg/dl and lowering TG levels by 5.03.8 mg/dl.

2.5.2 Effect of Exercise Training on Cholesterol

Cholesterol is a waxy substance made by animal liver and also supplied in diet through animal products such as meat, poultry, fish and dairy products. Cholesterol plays a major role in human heart health. High cholesterol in serum is a leading risk factor for human cardiovascular diseases, such as coronary heart disease (CHD) (Consumer Union, 1998; Wildman & Miller, 2004, Williams, 2007).

Researches have shown that aerobic exercise training is believed to reduce the risk of cardiovascular disease partially through increasing serum levels of HDL-C (Kelley, Kelley, Vu Tran,; 2004; American Heart Association, 1997). However, this effect varies considerably among exercise intervention studies. The National Cholesterol Education Program (NCEP) was developed with the general goal of reducing the prevalence of high serum cholesterol in the United States. A borderline – high (200-239 mg/dl or high (<240 mg/dl) have been reported by the American Diabetic Association, (2005).

Several studies have indicated that cholesterol levels can be reduced through exercise training. Tolfrey *et al*; (2000), reported that trained or active children and adolescents demonstrate favorable levels of HDL-C, total cholesterol/HDL-C and LDL-C/HDL-C, whilst total cholesterol is generally unaffected. Kelly *et al*; (2005), reported that across all categories (340 exercise, 265 control), random effect modeling resulted in statistical significant improvement for Total Cholesterol (TC), but not HDL and LDL. Guo *et al*; (2011) observed that based on the World Health Organization Quality of Life – 26 (WHO-QOL-26) Score, TG, TC, HDL-C and LDL-C had improved significantly at the end of three months of exercise. Habibzadeh (2010), reported that TC, TG, FBS significantly decrease ($P<0.05$) in a 2 months walking exercise in young obese women. Narayani & Sudhan, (2010), have similarly shown that an isolated walking training programme for obese women for 45 minutes a day decreased body percent fats, TC and increased HDL.

2.5.3 Effect of Exercise Training On High Density-Lipoprotein-Cholesterol (Hdl-C)

HDL is a protein complex in the blood that facilitates the transport of 45-50% of moderate amount of cholesterol and phospholipids and very little triglycerides. HDL-C- is a medium through which cholesterol is transported on the blood. HDL levels are protective against CHD and diabetes. HDL transport cholesterol from peripheral cells to the liver, known as cholesterol transport (Brouns & Cargill, 2002).

The precise biochemical mechanisms underlying the beneficial effect of exercise on serum lipids have not been identified. Researchers have found that in trained males and females, activity of several enzymes such as hepatic lipase and apoprotein lipase, are modified in such a way as to promote a more catabolism of triglycerides and a greater production of high density lipoprotein (Durstine et al; 2002; Williams, 2007). The positive effects of exercise training include raised HDL-C levels and reduced TG levels (Leon & Sanchez, 2001). According to Venkateswarlu (2010), moderate jogging or brisk walking for about 30 minutes, 3 – 5 times a week, is necessary to produce improvement in HDL-C. At the minimum level of exercise, changes in HDL-C and TG levels are sometimes small and unpredictable, but exercise programme of longer duration (45 minutes or longer), higher intensity and more frequency, produce much more positive effects on HDL-C and TG.

Regular endurance exercise is a widely recognized modality to raise plasma HDL cholesterol levels which is one of the metabolic adaptations contributing to the reduced risk of CHD observed among physically active and fit individual (Blair, Kohl, Paffenbarger, Clark, Cooper & Gibbons 1989; Folsom, Ameti, Hutchinson, Liao, Clegg & Cooper, 1997). Although a low plasma HDL-C concentration is often accompanied by an elevated TG level associated with abdominal obesity and an insulin resistance-hyperinsulinemia state (Despres, 1994). Some individuals are characterized by low HDL-C level without obesity or hypertriglycemia, a condition called isolated hypoaphalipoproteimia (Goldbourt, Yaari & Medalic, 1997, Lavie et al; 1992). Studies have suggested that patient with isolates low HDL-C syndrome may be at increased CHD risk (Goldburt et al; 1997).

Several studies have reported various changes in HDL-C following exercise training. Thompson, Adeniran & Sady, (2001), observed that acute exercise may reduce blood pressure and serum TC, increase HDL-C and improve insulin sensitivity and glucose homeostasis. Exercise training prevents and alternates the decrease in HDL-C but when combined with omega-3 fatty acid supplementation, may actually increase serum HDL-C (Thomas *et al*; 2004). Gallian & Burk (1978), in a six-week study using aerobic activities for 35 minutes per session, observed a significant ($P<0.05$) increase in HDL-C levels with no change in total cholesterol (TC). Linder, Durant & Mahauney, (1983), after an eight week walk/jog program on 29 boys aged 11-17 years, observed no training effect on HDL-C. They attributed that the study was faced with the problem of different maturation ages. Blessing, Keith & Williford, (1999), observed positive effect in HDL-C, TC/HDL-C levels after a 16 week training program involving males and female 13-18 years. Stergiouslos, (1998), examined the effect of aerobic training load on HDL-C in 18 boys aged 10-15 years. HDL-C levels increased significantly ($P< 0.05$) after eight weeks training programme. Muhammad (2003) in an assessment of the effect of aerobic exercise on selected physiological variables in non-dependent diabetics, observed an increase in HDL-C after 12 weeks of bench-step exercise training. Durstine *et al*; (2001) in a meta-analysis of well controlled studies, indicated that an exercise volume of 1200-2200 calories per week is often effective at elevating HDL-C levels from 2-8 mg/dl and lowering TG levels by 5-3.8 mg/dl. Adeyanju (2002), observed a significant sex-specific increase in HDL-C ($f-34.54 < 0.05$), as effects of continuous and interval training.

Guo *et al*; (2011); reported a significant improvement in HDL-C at the end of three months aerobic training. Kelley *et al*; (2005); reported 3% change in HDL and 2% changes in TC as equivalent to improvement. Tolfrey *et al*; (2000); reported in their study that trained children and adolescent demonstrated favorable levels of high density lipoprotein- cholesterol (HDI-C). Jatau *et al*; (2012); reported considerable increase in HDL-C in experimental group from 29.4 $\pm$ 6.83mg before start of training to 42.39 $\pm$ 6.5 mg/ml after training.

Kodoma, Tanaka, Salto, Shu, Sone, Onitake, Suzuki, Shimano,Yamamoto,Kondooohashi, Yariada & Sone, (2007), reported a mean net change in HDL-C level which was statistically significant but modest (2.53 mg/dl (0.065 mmol/L $P < .001$). They concluded that regular aerobic exercise modestly increases HDL-C.

2.5.4 Effect of Exercise Training on Low Density Lipoprotein-Cholersterol (Ldl-C)

Classification of lipoprotein may be determined by several methods based on their densities. Designation ranges from high to very low density. A wide variety of lipoprotein exists based upon the specific lipid and protein content (Wildman & Miller, 2004). LDL- is a protein lipid complex in the blood that facilitates the transport of cholesterol, triglycerides and phospholipids (Brouns & Cargill, 2002; Vantone, 2002). LDL-C is a mechanism whereby cholesterol is transported in the blood. High blood levels cholesterol are associated with increased incidences of CHD and diabetes (American Heart Association, 1997; Graig, 1998).

Many types of exercise training appear to positively influence blood lipid profiles. Positive changes related to exercise training include reduction in TC, LDL-C levels, raised HDL-C levels and reduced TG levels (Thomas, Adeniran & Etheridge, 2004). Researchers have used cross-sectional design to assess dose-response relationship between the volume of exercise and changes in blood lipid levels (Drygas, Kostka, Jegier, & Kunski, 2000). Linder, *et al*; (1983) examined the effect of an eight week walk/jog programme at a HR intensity of 80% of peak HR on 29 boys aged 11-17 years and reported training effect on LDL-C. Blessing *et al*; (1995), in a 16-week training programme involving males and females 13-18 years for 40 minutes in various aerobic activities at an intensity of 90%, observed positive alterations in LDL-C levels after the exercise training period. Muhammed (2003), assessed the effects of aerobic exercise on selected physiological variables on non-insulin dependent and reported a decrease in LDL-C which indicates a significant difference in LDL-C ($t = 6.38$). To find out the effects of 12 week continuous and interval training protocol, on body composition variables and Lipoprotein profiles,

Adeyanju, (2002), observed significant effects of training on LDL-C by training groups. LDL-C (F29.751 4.05). Similarly, Kelley, *et al*; (2005), observed a 0.3% change in LDL-C which have equivalent to improvement following the use of meta-analytic approach to examine the effects of aerobic exercise on lipids and lipoprotein in overweight and obese adults.

Tolfrey *et al*; (2000) reported that trained or active children and adolescents demonstrated favorable levels of LDL-C. Guo *et al*; (2011), reported significant improvement of LDL-C at the end of three months of aerobic exercise. Jatau, Venkateswarlu, Dikki & Haruna, (2012), assessed the effects of moderate intensity interval training in running on lipid and lipoprotein profiles of sedentary Nigerian male adults and reported a significant difference between experimental and control groups after 12 weeks training on LDL-C, but did not report any significant decrease on LDL-C in the experimental group.

2.5.5 Experimental Studies on the Effect of Exercise Training on Lipids (Triglycerides, and Cholesterol) and Lipoproteins (Low Density Lipoprotein and High Density Lipoproteins)

Studies conducted have always combined lipids and lipoproteins together. In the light of this, summary of experimental studies will be given in similar forms. There is interest in how altered lipid metabolism could contribute to muscle insulin resistance. Many animal and human states of insulin resistance have increased muscle triglyceride content, and there are now plausible mechanistic links between lipid accumulation and insulin resistance, which go beyond the classic glucose fatty acid cycle (Griffin, 1999; Bell, 2000; Hegarty *et al;* 2003).

Tolfrey *et al*.;(2000), investigated the effect of aerobic exercise training on the lipid lipoprotein profile of children and adolescents. Cross sectional comparisons of dichotomized groups provide the strongest evidence of exercise effect. Trained or active children and adolescents demonstrate favourable levels of high density lipoprotein-cholesterol, triglyceride, total cholesterol, HDL-C and LDL-C, whilst TC is generally unaffected. They concluded that recent studies have suggested that increase in HDL-C and reductions in LDL-C may be possible with regular exercise. The identification of a dose

response relationship between exercise training and the lipoprotein profile during the pediatric years remains elusive.

Kelley *et al*; (2005), used the meta-analytic approach to examine the effects of aerobic exercise on lipids and lipoprotein in overweight and obese adults. In their study, selections were randomized controlled trials; (aerobic exercise > or = 8 weeks; adult human > or 18 year of age; all subjects overweight or obese, BMI > or 25 $kg/m^{(2)}$) assessment of one or more of the following lipid and/or lipoprotein variable: total cholesterol (TC), high-density lipoprotein variable: total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG). Results of this study showed that in total, 13 studies representing 31 groups (17 exercise, 14 control), 613 subjects (348 exercise, 265 control), and up to 17 outcomes were available for pooling. Across all categories, random effects modeling resulted in statistically significant improvements for TC (X$\pm$ s.e.m., - 3.l4 $\pm$ 1.7mg/ol; 95 % CL, - 6:7 to 0.2 mg/dl) and TG (X $\pm$ s.e.m., - 16.1 $\pm$ 7.3 mg/dl, 95% cl., - 30.2 to -2.1 mg/dl) but not HDL (x $\pm$ s.e.m., 1.6 $\pm$ -0.8/dl, 95% C.L., - 0.02 to 3.2 mg/dl) or LDL (x $\pm$ s.e.m. – 0.5 $\pm$ 1.3 mg/dl, 95% CL, -3.0 to 2.0 mg/dl). Changes were equivalent to improvements of 2% (TC), 11% (TG), 3% (HDL) and 0.3% (IDL). After conducting sensitivity analyses (each study deleted from the model once), only decreases in TG remained statistically significant. Increase in HDL were associated with increases in maximal oxygen consumption (Vo_2 max. in ml/kg/min, r = 0.75, P = 0.002) and decreases in body weight (r = 0.77, P < 0.001), while decreases in LDL were associated with decreases in body weight (r = 0.75, P = 0.009). They concluded that aerobic exercise decreases TG in overweight and obese adult. However, a need exist for additional randomized controlled trials in various overweight and/or obese populations above and beyond those included in the analysis.

Aerobic exercise is believed to reduce the risk of cardiovascular disease partially through increasing serum levels of high density lipoprotein cholesterol. However, this effect varies considerably among exercise intervention studies. Kodama *et al*; (2007), in their study, used the electronic database searches of Medline Plus (2012), for randomized controlled trials that examined the effect of exercise

training on HDL-C level. Results of the study showed that twenty five articles were included. Mean net change in HDL-C levels was statistically significant but modest (2.53 mg/dl [0.065 mmol/L] $P < 0.001$). Minimal weekly exercise volume for increasing HDL-C level was estimated to be 900 kcal of energy expenditure per week or 120 minutes of exercise per week. Univariate regression analysis indicated that every 10 minute prolongation of exercise per session was associated with an approximately 1.4 mg/dl (0.036-mmol/L) increase in HDL-C level. In contrast there was no significant association between exercise frequency and intensity. Multiple meta-regression analysis demonstrated that subject with BMI less than 28 and total cholesterol level of 220 mg/dl (5.7 mmol/L) or more experienced and approximately 2.1 mg/dl (0.054-mmol/L) larger increase in HDL-C level than those with BMI of 28 or more and total cholesterol level less than 220mg/dl (5.7 mmol/L). They concluded that regular exercise modestly increases HDL-C level.

The metabolic, syndrome is characterized by the accumulation of several metabolic risk factors. It is important to improve physical activity and dietary habits to reduce the risk of cardiovascular disease in humans. In consideration of these risk factors, Guo *et al*; (2011), studied the effect of aerobic exercise on lipid profiles and high molecular weight adiponectin in Japanese workers. The study participants participated in a weekly aerobic exercise programme that included a session composed of a brief meeting, warm-up exercise, and primary exercise (low and high impact, stretch, muscle training, and cooling down). To evaluate the effect of this intervention they measured body fat composition, holding power, and quality of life assessment. Blood tests were also carried out before and every 3 months during the study. Findings revealed that of the 37 participants enrolled in the exercise group constituted of 42 subjects, 36 (85%) of whom were available for follow up at the end of the 12 week study period. In the exercise group, weight, body fat percentage, waist circumference, the World Health Organisation quality of life 26 (WHO QOL 26) score, triglyceride, total cholesterol, high density lipoprotein cholesterol and low density lipoprotein cholesterol had improved significantly at the end of

three months. They concluded that aerobic exercise led to an improvement in body composition and lipid profiles.

Muhammad (2003, studied the effects of aerobic exercise training on selected physiological variables in non-insulin dependent diabetics. Effects of aerobic training, using bench step as a mode of exercise on non-insulin dependent diabetics were studied involving 90 male non-insulin dependent diabetic subjects between the ages of 40 and 60 years. Two groups research design was used. 45 non-insulin dependent diabetics were used as experimental group while 45 were used as control group. The experimental group was subjected to bench steps as a mode of exercise training at an intensity of 65 – 70% maximal heart rate for 30 minutes; 3 alternate days a week for twelve weeks, while the control group did not undergo any prescribed training throughout the 12 weeks. Resting heart rate, fasting blood sugar, blood pressure and lipid profiles were measured before the training commenced, fortnightly throughout the training period, and at the end of the 12 week of exercise training. Results of the study revealed that baseline values for LDL-C were, Control =4.57 $\pm$ 47; Experimental= 4.78; and following 12 weeks training were, control= 4.73 $\pm$ .32; Experimental= 3.83 $\pm$ .45; HDL-C, baseline values, Control 1.32 $\pm$ .25, Experimental 1.03 $\pm$ .11; and after 12 weeks values were Control 1.43 $\pm$ 2.4 and Experimental 2.03 $\pm$ .12; TC baseline values were Control 5.94 $\pm$ .51, Experimental 6.60 + .33, after 12 weeks values were Control 6.08 + 42, Experimental 4.38 + .25; and TG baseline values were, Control 2.43 + .22, and Experimental 3.15; and after 12 weeks training, control 2.39 + .3 and Experimental 1.50 + .12. This result revealed a significant decrease in low density lipoprotein, triglycerides and total cholesterol, and a significant increase in high density lipoprotein cholesterol due to 12 weeks bench step exercise training. It was concluded that aerobic training using bench step as a mode of exercise at an intensity of 65-70% maximal heart rate for 30 minutes, 3 alternate days a week for 12 weeks improved physiological fitness and reduced the risk of related heart disease in non-insulin dependent diabetics. Moderate to vigorous physical activity have been shown to have positive effect on lipids and lipoprotein levels of both male and female adults.

In another study, Jatau *et al*; (2012), investigated the effect of moderate intensity interval training in running on lipids and lipoprotein of sedentary Nigerian male adults. To achieve the purpose of the investigation, a 2 x 3 factorial design was used in which thirty sedentary male participants aged between 20-30 years were randomly assigned to either experimental or control group (15 each) who were tested three times during the period of the investigation (Week 0, six, and twelve). The study was limited to TC, TG, HDL-C and LDL-C. The study revealed the following results: Baseline values for TC; Control 140.97 ± 29.9, Experimental 130.23 ± 20.3 mg/dl; after 12 weeks training values – Control = 136 ± 32.99, Experimental 128.15± 19.87; TG baseline values, Control 42 ± 9.57, Experimental 58.59 ± 23.29, after 12 week training values Control = 75.9 ± 28.03, Experimental 57.3 ± 5.65 mg/l; HDL-C baseline values, Control 30.14 + 14 + 4.63 Exp. 29.45 + 6.83 mg/l, after 12 weeks training values, Control, = 41.22 + 7.08, Experimental 42.39 + 6.51 mg/l, at LDL-C baseline values, Control – 19.82 + 6.14, Experimental 14.12 + 3.18 mg/l, after 12 weeks training values, Control 12.99 + 5.27, Experimental 14.45 + 4.71 mg/l. The result of the study indicated that moderate intensity interval training does not significantly affect the serum levels of lipids and lipoprotein of sedentary male Nigerian adults. It was concluded that there is need for increase in either duration or intensity to bring about desired effects. HDL-C baseline values, Control 30.14 ± 14 _ 4.63 Experimental 29.45 ±6.83 mg/l., after 12 weeks training values, Control 41.22 ± 7.08, Experimental 42.39 ± 6.51 mg/l. at LDL-C baseline values, Control 19.82 _ 6.15, Experimental 14.12 ± 3.18 mg/l, after 12 weeks training values, Control 12.99 ± 5.27, Experimental 14.45 ± 4.71 mg/l. The results of the study indicated that moderate intensity interval training does not significantly affect the serum levels of lipids and lipoprotein of sedentary male Nigerian adults. It was concluded that there is need for increase in either duration or intensity to bring about desired effects.

Regular endurance exercise training is a widely recognized modality to raise plasma HDL-C (Despres *et al*; 1994; Wayo, Gwani, Chado & Haruna, 2012), which is one of the metabolic adaptations contributing to the reduced risk of coronary heart disease (CHD), observed among physically active and

fit individuals (Blair *et al*; 1989; Folsom *et al*; 1997; Leon & Sanchez, 2001). Although a low plasma HDL-C concentration is often accompanied by an elevated triglyceride (TG) level associated with abdominal obesity and an insulin resistance-hyperinsulinemic state (Despres, 1994). Some individuals are characterized by low HDL-c levels without obesity or hypertriglyceridemia, a condition referred to as hypoalphalipoproteinemia (Lavie, Mailander & Milani, 1992; Goldsbourt *et al*; 1997). Previous study by Lamarche, Despres, Pouliot, Prud'homme,Moorjani,Lupine, Nadeau, Tremblay & Bouchard, (1993), showed that subjects with isolated HDL-C were neither characterized by hyperinsulinemia nor visceral obesity. In their study, the effects of endurance exercise training on plasma HDL-C levels depend on levels of triglycerides.

Couillard, Despres, Jean-Pierre, Kamarche, Bergeon, Gagnon, Leon, Rae, Skinner, Wilmore & Bouchard, (2001), compared the response of numerous lipoprotein/lipid variables to a 20-week endurance exercise training program in men categorized on the basis of baseline TG and low HDL-C concentration : 1) low TG and high HDL-C (normolipidemia), 2) low TG and low HDL-C (isolated HDL-C), 3) high TG and high HDL-C (isolated high TG), and 4) high TG and low HDL-C (high TG/low HDL-C). Series of physical and metabolic variables were measured before and after the training program in a sample of 200men enrolled in the Health, Risk, Factors, Exercise Training and Genetics (HERITAGE) Family Study. At baseline, men with high TG /low- had more visceral adipose tissue than did men with isolated low HDL-C and men with normolipidemia. The 0.4% (not significant) exercise –induced increase in HDL-C levels in men with isolated low HDL-C suggests that not benefit from the 'HDL-raising' effect of exercise. In contrast, men with high TG/low HDL-C showed significant increase in HDL-C levels (4.9%, P<o.o05). Whereas both subgroups of men with elevated TG levels showed reduction in plasma TGs (= ~15.0,P<0.005), only those with high TG/low HDL-C showed significantly reduced apolipoprotein B levels at the end of the study (~ 6.0%,P<0.005). Multiple regression analyses revealed that the exercise–induced change in abdominal subcutaneous adipose tissue (10.6%, P< 0.01) was the only significant correlate of the increase in plasma HDL-C with training in men with TG/ low HDL-C. Results of the study

suggests that regular endurance exercise training may be particularly helpful in men with low HDL-C, elevated TGs and abdominal obesity

2.6 Summary

Glucose transport being the rate-limiting step in muscle glucose utilization is carried out by the glucose transport protein present on the cell membrane. An increase in insulin responsiveness results in a large increase in glucose transport in maximally effective insulin stimulus with a proportional upward shift of the dose response curve. It is well established that GLUT4 translocation is an important cellular mechanism through which exercise enhances skeletal muscle glucose uptake. In high serum glucose, physical activity may improve insulin sensitivity and assist in diminishing blood glucose levelsinto normal range. Studies have strengthened the importance of log- term physical activity programs for thetreatment and prevention of hyperglycemia, a common metabolic abnormality and its complications.

The principal purpose of physical exercise for the primary prevention and treatment of lifestyle related disease is to reduce insulin resistance. Insulin action and glucose transport is characterized in terms of insulin sensitivity and insulin responsiveness that is the concentration of insulin required to cause 50% of its maximal effect on glucose transport.

Insulin being the most important hormone that is concerned with the regulation of carbohydrate metabolism and body sugar level, is the only antidiabetic hormone secreted in the body by the beta cells. In carbohydrate metabolism, about 32% of glucagon is degraded in liver and 20% in kidney. The primary regulator of plasma glucagon is the circulating glucose. A drop to 3.7 mol/L or 67mg/dl in plasma glucose potent is stimulus for glucagon secretion from the alpha cells of the pancreas.. Insulin resistance is the inability of circulating insulin to exert a normal physiological effect at a target tissue classically described as impaired insulin stimulated skeletal muscle uptake. Insulin

resistance or impaired biological response to circulating insulin is a disorder common to glucose intolerance, obesity, dyslipidemia, hypertension and cardiovascular disease.

Glucagon increases gluconeogenesis in liver and does not induce glycogenolysis in muscles. Insulin and glucagon are hormones that work to regulate the level of sugar in the body and to keep it under healthy range. The coordinated action of insulin and glucagon shows that an increase in insulin level inhibits glucagon release from alpha cells. Exercise plays an important role in the regulation of insulin within the body. With exercise, insulin is not readily released from pancreas due to the lower blood glucose levels. During exercise, plasma insulin concentration showed a decline from basal level with the onset to the end of exercise. With increase exercise duration, the amount of cortisol secreted increases in order to preserve plasma glucose with resultant increase in glucagon to promote gluconeogenesis.

Many types of exercise appear to positively influence blood lipid profiles, such as reduced TG levels. High cholesterol in serum is a leading risk factor for human cardiovascular disease, such as coronary heart disease (CHD). Several studies have indicated that cholesterol levels can be reduced through exercise training. LDL is a protein complex in the blood that facilitates the transport of cholesterol, triglycerides, and phospholipids. Many types of exercise appear to positively influence lipid profiles. Such positive changes related to exercise include reduction of TC, LDL-C levels, raised HDL-C levels and reduced TG levels. HDL-C is a mechanism whereby cholesterol is transported on the blood. HDL levels are protective against CHD and diabetes. HDL transport cholesterol from peripheral cells to the liver, known as cholesterol transport. The positive effects of exercise training include raised HDL-C levels and reduced TG levels.

CHAPTER THREE

3.0 RESEARCH METHODOLOGY

3.1 Introduction

The purpose of this study was to find out the effect of aerobic training on serum glucose, insulin, glucagon, lipids and lipoproteins of overweight Nigerian male adults. The research design, population, sample and sampling techniques, the training protocols, tests and statistical techniques used to achieve this purpose of the study are described in this chapter.

3.2 Research Design

For the purpose of this study, an experimental design usining one group repeated trials research design was used for this study.With this design, one group was given different treatments at different times. The baseline or pre-training measures served as control while the 6^{th} week and 12^{th} week measures were the experimental manipulations. In this design, the same group of subjects was given several tasks of different complexity or experimental manipulation. The design was used to maximize the between treatments variance, identify the beween units variance and to maximize the error residual variance (Kerlinger, 1988; Oladele, 2007).

3.3 Population

The population for this study comprised of 302 male students of ECWA Health Technology, Kagoro (ECHTK), between the ages of 25 and 35years as at April 2014. This record was abtained from the office of the students' affairs officer of the ECHTK.

3.4 Sample and Sampling Techniques

A purposive sampling of weight and height of Nigerian male adults who were students of ECHTK was carried out. Students whose BMI were between 25.0 kg/m^2 and 29.9 kg /m^2 were identified and

were briefed regarding the purpose of this research. Only 48 male adults met the inclusion criteria and after the briefing, 25 persons volunteered to participate in the program.

3.5 Training Protocol

All subjects for this study underwent continuous walking and jogging program on 3 alternate days a week for 12 weeks.

Intensity of training was monitored using the Borg & Linderholm, (1969); Borg (1998), perceived rate of exertion (RPE) scale shown below

Rating	Intensity
6	No exertion at all
7-8	Extremely light
9-10	Very light
11-12	Light
13-14	Somewhat hard
15-16	Hard
17-18	Very hard
19	Extremely hard
20	Maximal

Training commenced at RPE of 9-10 (very light) at intensity of 40-45% HR max of each participant. All the participants walked for 15 minutes and jogged continuously for 10 minutes. This was

followed with a 5 minutes stretching and cool down activities. This training duration and intensity lasted for 3 weeks.

At the beginning of the 4^{th} -6^{th} week, training intensity was maintained at RPE 11-12 (light) corresponding with 45-50% HR max of each participant. During this phase, all participants walked for 15 minutes, jogged for 15 minutes and ending up with 5 minutes stretching and cool down activities.

From weeks 7-9, training intensity was monitored at RPE 13-14 (somewhat hard), corresponding with 50-55% HR max of the participants. During this phase, they first walked for 15 minutes and jogged for 25 minutes with a cool down/ stretching activities of 5 minutes.

During the 10^{th} -12^{th} week training, RPE of 15-16was monitored at 55-60% HR max. The participants walked and jogged for 20 minutes and 25 minutes respectively with cool down and stretching activities of 5 minutes.

The training schedules used is shown in the table below

Table 1 Training schedule designed and used by the researcher.

Period	Aerobic ACTIVITIES		Cool Down	Total Duration	Intensity(HR/max)	RPE
	Walking	Jogging				
0-3wks	15min	10min	5min	30 min	40 - 45%	9-10
4-6wks	15min	15min	5min	35 min	45 - 50%	11-12
7-9wks	15min	20min	5min	40 min	50 - 55%	13-14
10-12 wks	20min	25min	5min	50 min	55 - 60%	15 – 16

Wks = weeks

Training was conducted three (3) times per week on alternate days. All participants were trained on how to rate the training intensity. The participants taught how to use the RPE and were

constantly asked how they perceived the exertion through each training phase as recommended by Dishman, (1994); Wilmore & Costill, (2004); McArdle, Katch, & Katch, (2010).

3.6 Experimental Requirements

3.6.1 Research Assistants

Three research assistants consisting two laboratory technicians, and one Physical Education teacher, were recruited and briefed about the experiment before the commencement of data collection.

The laboratory technicians assisted in taking and preserving blood samples for further laboratory analyses, while the physical education teacher assisted the researcher in measuring height and weight of the subjects.

The researcher commenced the training of the participants after all baseline data was collected. The researcher personally administered and supervised training program from the beginning to the end.

3.6.2 Informed Consent

All participants were made to fill an informed consent form. Participants involved in the study were adequately briefed on the procedures of the experiment, the likely benefits to be derived from participation, the discomfort to be experienced, and the precautions to be taken for hitch-free participation in the training program, before completing and signing the informed consent form (Appendix C).

3.6.3 Ethical Permission

A formal request to use human subjects for the study was sought and obtained from the Ethical Committee of the School of Post-Graduate Studies, Ahmadu Bello University, Zaria (Appendix A). A letter of introduction from the Department of Physical and Health Education, Faculty of Education,

Ahmadu Bello University, Zaria, to the Provost ECWA Health Technology, Kagoro, was also obtained to introduce the researcher (Appendix B).

3.7 Instrumentation

The following research instruments were used in the study for data collection.

Measuring tape: Field tape/ ruler of non elastic horse brand, model S1542, made in China, were used to measure the height of each participant.

Weighing scale: A potable bathroom Hansen scale, (Model B10801A), made in Ireland, was used to measure weight in kilograms (AAHPERD 1990; WHO, 1999; Baumgartner, Jackson, Mahar & Rowe, 2007). Each participant's weight was measured to the nearest 0.5kg.

Stop Watch:, (airtour1/5), was used to time duration of workout to the nearest second on each training day (Baumgartner *et al*; 2007).

For the collection of blood sample and biochemical analyses, the following instruments were used.

Fluoride oxalate container: for storage of blood samples

Tourniquet, Disposable syringe and needle (CE 0318-0.8mm x 40mm) was used to obtain blood samples from subjects by direct venupuncture; Centrifuge as used to centrifuge blood); Spectrophotometer was used to read analyses of glucose, triglyceride, cholesterol, HDL-C, LDL-C and HDL-TG, while Micro plate reader was used to read insulin and glucagon)

3.8 Physical Characteristics f Subjects

Subjects' physical characteristics (height and weight) were assessed in accordance with the protocol of International Working Group on Anthropometry (IWGK) as described by Ross & Marfell-Jones, (1982). Specifically, measurements included standing height and weight.

Height: Subjects' height was measured while standing erect looking straight ahead and bare-footed against the stadiometer. Horizontal broad blade wooden ruler was rested on the head of each subject against the instrument to the nearest 0.1cm.

Weight: subjects' weight was measured using a portable bathroom scale with provision for re-calibration while dressed in light dress without footwear. The weight was recorded to the nearest 0.5kg

Body Mass Index (*BMI*): The height and weight measures were used to calculate the body mass index by dividing weight in kilograms by height in meters squared (wt/ht^2) (Heyward, 1997; WHO, 1998; 1999; Wildman & Miller, 2004; Baumgartner *et al*; 2007; Williams, 2007; Plowman & Smith, 2008).

3.9 Biochemical Measurements

Sugar (serum glucose) analysis for fasting blood sugar, insulin sensitivity, glucagon suppression, lipids and lipoproteins analyses were carried out at the Chemical Pathology Laboratory, Ahmadu Bello University Teaching Hospital (ABUTH) Zaria. The baseline, after 6^{th} week, and 12^{th} week training blood samples were taken between 8.00 a.m. and 10.00 a.m, following the procedures descrbed by Frankel, Elwood & Sweetum, (1996).

The Chief Chemical Pathologist, ABUTH, Zaria, read and approved that the principles, procedures, reagents and calculations for the determination of the variables used for this study were within chemical laboratory recommendations.

To collect blood samples for laboratory analysis procedure, a tourniquet was tied around subject's left upper arm to ensure a brief arrest of circulation to the forearm. Subjects were instructed to clench their fist in order to increase the prominence of the antecubital vein from which blood was

drawn. About 5 milliliters of blood was drawn by venupuncture from the antecubital of the left forearm with minimal statistics.

3.9.1. Bleeding and Conveyance of Blood Samples.

The bleeding was carried out with a 10 ml syringe under strict antiseptic conditions and transferred into numbered test tubes in test tubes racks. The blood samples were allowed to coagulate within two-hours of venupuncture and preserved after separation at General Hospital Kafanchan. Assay of blood glucose (FBS), lipids (triglycerides and cholesterol) and lipoproteins (LDL-C and HDL-C) was conducted at the Prestige Medical Laboratory Kafanchan. The separated serum was conveyed in cold-chain to the chemical laboratory for hormonal assay of serum insulin sensitivity and glucagon levels. The serum total cholesterol concentration (TC), high density lipoprotein -cholesterol (HDL-C) low density lipoprotein- cholesterol (LDL-C), and high-density lipoprotein- triglycerides (HDL-TG) tests were determined indirectly as described below.

3.9.2 Chemical Pathology Principles

The principles below guided the chemical pathologists in the estimation and assay of serum glucose, insulin, glucagon, lipids (triglyceride and cholesterol) and lipoprotein (LDL, and HDL)

3.9.3. Determination of Glucose

Principles

Glucose oxidase oxidizes the specific substrate B-D glucose, to gluconic acid and hydrogen peroxide was generated. Hydrogen peroxide thus produced is acted upon by peroxidase and oxygen liberated. The liberated oxygen is transferred to chromogen system consisting of 4-aminoantipyrine and phenolic compound to produce red quinoneimine dye. The intensity of colour is directly proportional to the concentration of glucose and is measured specific spectrophotometrically at 505 nm (505-540 nm or with GREEN filter) using oxidase. The reflometric method is a simple enzyme method in

which oxidase peroxidase enzyme and colour reagent are impregnated on the reagent stripes. This method uses a reflect check meter to register the amount of glucose in the blood.

Procedure

Reagent Stability Specimen:

Blood sample collected with any one of the anticoagulants like fluoride oxalate, EDTA, heparin or without any of the anti-coagulants can be used. To prevent glycolysis and better accuracy separations of serum or plasma, as soon as possible is necessary

Reagents

Prepare the working reagent as mentioned on label. Working reagent is stable up to 7 weeks when stored at 2-8^{0}c stable.

Reagent volume – 1.0mg

Volume – 1.0 ul

Light path – 1.0cm

Zero settings – Reagent blank

Calculation

$$\text{Glucose concentration mg/dl} = \frac{\text{Abs of test}}{\text{Abs of STD}} \times 100$$

To convert mg/dl to mmol/l, the following factor 1mmol/l = 18mg/dl; 1mg/dl = 0.056mmol/l is used (Rochalu, Bernt & Grabber, 1974; Reckon Diagnostic, 2003).

3.9.4 Determination of Insulin

Principles of Assay

This enzymes immunoassay (EIA) is based on the competition between unlabeled insulin and acetylcholinestrase (ACHE) linked to insulin (tracer) for limited specific insulin antiserum sites.

The complex antiserum insulin (free insulin or tracer) binds to antibody that is attached to the well. The plate is then washed and Ellman's reagent (enzymatic substrate for ACHE and chromogan) is added to the wells. The ACHE tracer acts on the Elliman's reagent to form a yellow compound.

The intensity of the colour, which is determined by spectrophotometer, is proportional to the amount of tracer bound to the well and is inversely proportional to the amount of free insulin present in the wall during the immunological incubation.

Procedure

It is recommended to perform the assay in duplicate and to follow the instructions hereafter.

Plate preparation- prepare the ash buffer

Open the plate and select the sufficient strips for the assay and place the unused strips in the packet (stored at 4^{o}c). Rinse each well five times with the buffer (300µc/well). Just before distributing reagent and samples, remove the buffer from the wells by inverting the place and shaking out the last drop.

Reagent

The coated micro liter plates and reagents are provided ready to use. E/A buffer reconstitute one vial with 50ml of distilled or deionized water. Allow it to stand 5 minute until completely dissolved and then mixed thoroughly by gentle inversion. Stability at 4^{o}c: 1 month

The concentration of the first standard is 10ng/ml. Prepare seven propylene tubes (for the seven other standards) and add 500µc of EIS buffer into each tube, add 500µc of the first tube

(containing the first standard) to the second tube, continue this procedure for the other tubes. Thus, standard concentrations are 10(51), 5(52), 2.5(53), 1.25(54), 0.64(55), 0.31(56), 0.16(57) and 0.08ng/ml (58), respectively. Stability at 4^{o}c: 1 day (Grassi & Pradellis, 1991)

Reagents include heptane, isopronalol sulphuric acid (0.08N), sodium methylate, periodate reagent (sodium metaperiodate Na/04, 0.05ml), acetyl acetone reagent

Calculation

Subtract the absorbance readings off the blank well (absorbance of Elliman's reagent) from the absorbance reading of the rest of the plate.

Calculate the blank (B)/ maximum Binding BO (B/BO) for each standard point (y axis) versus the concentration (x axis). Draw a best fit line through the points (Reece & Campbell, 2002; Reckon Diagnostic, 2003; SPI-Bio, 2005).

3.9.5 Determination of Glucagon

Principle

The glucagon enzyme immunoassay (EIS) kit is an in vitro peptide based on the principle of competitive enzyme immunoassay. The microplate in the kit is pre-coated with anti- rabbit secondary antibody. After the blocking step and incubation of the plate with antiglucagon antibody, both biotinylates glucagon peptide and peptide standard or targeted peptide in sample interacts completely with the glucagon antibody. Uncompleted (bound) biotinylated glucagon peptide then interacts with streptavidim – hosradish peroxidase (SA-HRP) which catalyzes a colour development reaction. The intensity of cocorimetric signal is directly proportional to the amount of biotinylates peptide SA_PHR complex and inversely proportional to the amount of glucagon peptide on the standard or samples. This is due to the competitive binding to glucagon antibody between biotinylated glucagon peptide and

peptides in standard or samples. A standard curve of known concentration of glucagon peptide can be established and the concentration of glucagon peptide in samples can be calculated accordingly,

Procedure

Keep kit reagents on ice during reagent preparation steps. (All standard and samples be run at least in duplicate.

- Add (100µl of anti-glucagon antibody to each well. Incubate for 1.5 hours at room temperature with gentle shaking (1-2 cycles/sec) or incubate overnight at 4^{o}C.
- Discard the solution and wash wells 4 times with 1x Wash Buffer (200-300µl each). Washing may be done with a multichannel pipette or an automated plate washer. Invert plate and blot it against clean paper towel.
- Add 100µl of each standard positive control and sample into appropriate well. Include blank well. Cover well and incubate for 2.5 hours at room temperature with gentle shaking (1-2 cycles/sec). Or incubate overnight at 4^{o}C.
- Discard the solution and wash 4 times.
- Add 100µl of prepared HRP- streptavidin solution to each well. Incubate for 30 minutes of room temperature in the dark with gentle shaking (1-2 cycles/sec).
- Add 50/l of stop solution to teach well. Read obsorbance at 450 nm immediately.

Reagents

These include microplate reader capable of measuring absorbance at 450nm; precision of pipettes to deliver 2µl to 1ml volume; adjustable. 1-25ml pipette for reagent preparation; 100ml and 1litre graduated cylinder; absorbance paper; distilled or deionized water; sigmaplot software (or ottor software which can perform four-parameter logistic regression models). Tubes to prepare standard or sample dilution; orbital shaker; aluminum foil and saran wrap

Calculation

Calculate the mean absorbance for each for each set of duplicate standards. Controls and samples, and subtract the blank optical density. Plot the standard curve using sigma plot software (or other software which can perform four- parameter logistic regression models).

Percentage absorbance= (B – blade OD) (Bo – blank OD, where

B = OD of sample or standard

Bo = OD of zero standard (total binding)

(Grassi & Pradelles,1991; White,1999; Peace & Campbell 2002, Ochei & Okolhalkar, 2007, Sigman-Aldrich, 2013).

Absorbance

3.9.6 Determination of Triglycerides

Principles:

Lipase hydrolyses triglycerides sequentially to Dl and monoglyceride and finally to glycerol. Glycerol kinase (GK) using ATP as $P0_4$ source converts glycerol liberated to glycerol-3-phosphate (G-3-phosphate), G-3-phosphate oxidase (GPO) oxidase G-3-phosphate formed to dehydroxy acetane phosphate and hydrogen peroxide is formed. Peroxidase (POD) uses the hydrogen peroxide formed to oxidize 4-aminoentipyride and TODS (N – ethyl – N sulphohydroxy propyl in Toluidine) to a purple coloured complex. The absorbance of the colour complex is measured at 546 nm (530 – 70nm or with yellow filter) which is proportional to triglycerides concentration.

The enzymatic method for serum triglycerides involves the following steps.

Triglycerides are hydrolyzed by the enzyme lipase to produce glycerol and fatty acid. Triglycerides + H_2O ^{lipase}===➔ glycerole + fatty acids.

The enzyme glycerol kinase acts on glycerol in the presence of ATP to form glycerol-4-phosphate and ADP.

Glycerol

Glycerol + ATP ----------→ Glycerol 3- Phosphate + ADP

Kinase

Glycerol + 3 phosphate is oxidased by glycerol phosphate oxidase to dihydroxy acetone and hydrogen peroxide

Glycerol-3-phosphate+0_2

Glycerol – 3 – Phosphate oxidase dihydroxyacetone + H2 O2 1

Oxygen is released from H_2O_2 in the presence of peroxidase, which oxidases P-chlorohenrol chronogen to form a coloured compound.

H_2O_2 peroxidase $H_20 + 0_2$ + Pachlorophenol coloured product

Procedure

Fresh, clear fasting serum with no hemolysis should be used, herinised plasma may be used. No other anticoagulant is suitable. Serum level are slightly (.5mg/dl) higher than plasma level.

Pipette into test tube. Mix and incubate at 37^oc for 15minute and read absorbance of test and standard against reagent blank at 546nm (530 – 570nm or yellow filter)

Reagents

. Colour reagent Solution A: 100ml of phosphate buffer, Ph 7.2 contains

Lipase 30 units, glycerol kinase =1 0 units

Glycerol – 3 – Phsophate oxidase 5 units, peroxidase

5 units; stores at 2.8 ^{o} C

Solution B = Chloropenol: Dissolve 30mg in 100ml. distilled water. Store at 2-8^{o}C.

Colour reagent – Mix two parts of solution A with one part of solution B just before use.

Triglycerides standard (100mg/dl). Dissolve 100mg of triolein in 100ml

Mix well. Incubate at 37oC for 15 minutes. Read the absorbance test and standard against the blank at 420nm (violet filter).

Calculation

$$\text{Serum triglyceride mg/dl} = \frac{\text{Ab test}}{\text{Ab std}} \times 200$$

Serum triglyceride nmol/L = mg/dl x 0.043

Normal Values = Triglyceride: 80 – 150mg/dl (0.9 – 1.7 nmol/L). (Allain et al; 1974).

3.9.7 Determination of Cholesterol

Principles: The cholesterol esters are hydrolyzed to free cholesterol by cholesterol esterase (CE). The free cholesterol is then oxidized by cholesterol oxidase (CO) to cholesten 4-en-3-one with the simultaneous production of hydrogen peroxide. The hydrogen peroxide reacts with 4-aminoanti pyrine and phenolic compounds in the presence of peroxidase to yield a colored complex which is read at 505 nm.

Cholesterol esters CE →cholesterol + fatty acids

Cholesterol 0_2 CO → Cholesterol 4 en -3 one + H_2O_2.

$2H_2O_2$ + 4APP + phenolic compound] POD →Quinoneimine dye + $4H_2O$

The intensity of colour produced is directly proportional to the concentration of total cholesterol in the sample.

Procedure

Mix well and incubate for 10 minutes at 37^0c or 30minutes at R.T (25 ± 5^0c). Read absorbance of standard and test at 505nm (505 – 530) (green filter) against reagent blank.

Reaction parameter are type of reaction end point; wavelength =505; flow cell temperature=30^0c/37^0c; sample volume=1.0ml; incubation time=30m, RT/10 min;. Standard concentration=200mg/dl; setting with reagent blank.

Reagent

Enzopak cholesterol reagents are stable at 2.8^oc until the expiry date stated on the label. A special surfactant, Lipid Clearing Factor (LCF) is added to the reagent to solubilize the lepenuic (causing turbidity or opalescence) which adds to the accuracy of results (Allain, Poon, Chan, Richmond & Fu, 1974).

Calculation

Cholesterol concentration (mg/dl) = $\frac{\text{Absorbance}}{} \times 200$

3.9.8. DETERMINATION OF HDL – CHOLESTEROL.

Principle

High density lipoproteins (HDL) are separated from other lipoprotein fraction by treating serum with phosphotungstic acid and magnesium chloride. HDL remains in solution while all other lipoprotein fractions are precipitated. Cholesterol content is estimated by enzymatic method.

Working procedure –

For reagent stability and specimen, prepare the working reagent as mentioned on bottle label. Working reagent is stable up to 6 month at 2 – 8^{o}c. fresh clear serum under fasting condition with no hemolysis in the specimen of choice. Plasma collected using heparin as an anticoagulant may also be used.

Mix well and centrifuge at (3500-4000).rpm for 10 minute. Separate the clear supernatant immediately and determine cholesterol content. Mix well and incubate for 10 minute at 37^{o}c and read the absorbance of test and standard against reagent blank at 505nm (505-540 green filter)

Calculation

Serum HDL cholesterol – $\frac{\text{Abs of test}}{\text{Abs of std}}$ x conc of standard x dilution factor

___ $\frac{\text{Abs of test x 50 x 2}}{\text{Abs of std}}$

3.9.8 Estimation of Serum/Plasma HDL Cholesterol

Principle: HDL cholesterol is a negative risk factor for coronary heart disease (CHD). The risk of CHD increases as the value falls below 0.9 mmol/L and diminishes as levels become higher. HDL – reagent is produced by using a combination of detergents and phosphorous compounds which specifically bind LDL, VLDL and chylomicron (CM) but not HD1. The combination protects LDL, VLDL and CM from the

reaction by cholesterol esterase and cholesterol oxidase consequently HDL-cholesterol is selectively exposed to react with both enzymes.

HDL are separated from other lipoprotein fractions by treating serum with phosphotungstic acid and magnesium choleride, HDL remains in solution while all other

Reagents

Phosptungstic and reagen,t (PTA). Dissolve 4.5g phosphotungstic acid in about 50ml water. Add 16ml water.

Magnesium chloride, (2mm/L). Dissolve 40.6g of magnesium chloride (mgcl2 – 6H2O) in 100ml distilled water.

Tris buffer 10 mmol/Lm pH 7.6. Dissolve 1.21g in 90 ml distilled water. Adjust the pH to 7.6 with INHC and dilute to 100ml with distilled water.

Colour reagents, prepare as for method 2 above.

Concentrated suphuric acid.

Cholesterol standard (100mg/dl). Dissolve 100mg of pure cholesterol in 100ml glucine acetic acid.

Calculation

Serum HDL cholesterol (mg/dl) = $\frac{\text{Ab Test}}{\text{Ab std}} = 115$

Serum HDL cholesterol (mmol/L) = mg/dl x 0.025g

3.9.9. Estimation of Serum/Plasma LDL Cholesterol

Principle – Lipoprotein fractions are precipitated. Cholesterol content of which is estimated by enzymatic method. Chylomicrons, VLDL and LDL, are precipitated by phosphostic acid in the presence of magnesium ions leaving HDL in solution. The cholesterol content of the sunatel can be determined by suitable method.

Calculation

LDL cholesterol (mmol/L) = Total cholesterol = (HDL cholesterol + 0.46 x triglycerides) (All in mmol/L). (Grassi & Pradelles, 1991; Ochei & Okolhalkor, 2007; Sigman- Aldrich, 2013)

3.9.10 Statistical Analysis

For the purpose of this study, the following statistical techniques were used on data collected.

- Descriptive Statistics: This was to know the central tendency and viability values of the collected data (means, standard deviation, standard error and percent change) were computed to know the effect of training after 6^{th} and 12^{th} week of training. Mean changes achieved after 6^{th} and 12^{th} week aerobic training was computed as training effects.
- Repeated measures analysis of variance (ANOVA) statistics. This was used to determine significance difference between tests in each of the selected variables, as on group was involved in repeated trials at intervals from baseline, after 6^{th} and 12^{th} week of training
    - Post-hoc scheffe's test. To determine where significant difference occurred after 6^{th} and 12^{th} week of training/the phase of training that was responsible for difference.
    - An alpha level of 0.05 was used to retain or reject the null hypotheses raised for this study.

CHAPTER FOUR

4.0 RESULTS AND DISCUSSIONS

4.1 Introduction

The purpose of this study was to find out the effect of aerobic training on serum glucose, insulin, glucagon lipids and lipoproteins of overweight Nigerian male adults. The data collected for this study at baseline, after 6th and 12th week of training were analysed using the Statistical Package of Social Science (SPSS), version 17, at Iya Abubakar Computer Center, Ahmadu Bello University, Zaria.

This chapter presents the results of data analyzed and discussion of the findings.

4.2 Results

A total of 25 participants volunteered to participate in this study. During the period of the training program, 8 participants did not meet the required attendance of the three (3) times per week for 12 weeks and were excluded from the analysis. Only seventeen (17) participants met the required attendance and whose data were used for the analysis.

The physical characteristics of subjects at baseline, immediately after 6th and 12th week of training is presented in Table 4:2:1

Table 4.2.1a. Means, Standard Deviation (SD) and Standard Error (SE) of the Subjects' Physical Characteristics

Variable	Mean	SD	SE

Baseline	Age (Years)	34.12	7.75	1.88
	Weight (kg)	72.77	5.94	1.44
	Height (m)	1.65	.054	.01
	BMI (kg/m2)	26.84	1.82	.44
6th Week	Weight (kg)	71.77	5.58	1.35
	BMI (kg/m2)	26.28	1.70	.41
12th week	Weight (kg)	70.59	5.73	1.39
	BMI (kg/m^2)	25.81	1.82	.44

BMI = Body mass index

Table 4.2.1a. shows the means, standard deviation (SD) and standard error (SEE) of the physical characteristics of the subjects used for this study. An observation of the baseline data showed that the average age, weight, height and body mass index (BMI) of the subjects were 34.12±7.75 years, 72.77±5.94 kg, 1.65±.054m and 26.84 ±1.8 kg/m^2 respectively. The result of the BMI at baseline showed that the subjects were overweight.

As training progressed, the mean weight and BMI of the subjects reduced after 6th week (71.8 ±5.6kg and 26.3±1.7kg/m^2) respectively. Further reduction was observed also after 12th week in weight and BMI, (70.6±5.7kg and 25.8±1.82kg/m^2) respectively due to aerobic training

In order to find out whether the decreases in boby weight/ BMI were statistically significant, data were analysed using repeated measures ANOVA, the result of which is presented in table 4.2.1b

Table 4. 2.1b. Repeted measures ANOVA for differences in weight/BMI before, during and after 12 weeks of training.

Source	Type iii sum of squares	Df	Mean squre	F	Sig
Corrected model	1795.407a	2	897.7	5.283	.008
intercept					

training	47468.373	1	47468.4	279.350	.000
error	1795.407	2	897.7	5.283	008
	8156.356	48	169.9		
Total	57420.137	51			
Corrected total	9951.763	50			

F (2,48) = 2.6, P<0.05

Table 4.2.1b shows the results of repeated measures ANOVA on weight/bmi at baseline, 6th and 12th week of aerobic training. The result revealed significant effect of aerobic training on body weight/ of overweight Nigerian male adults. after 6th and 12th wweek of training (P>000).

TEST OF HYPOTHESES

Major Hypothesis

There are no significance effects of aerobic training on serum glucose, insulin, glucagon, TG, TC, HDL and LDL of overweight Nigerian male adults.

In order to find out if aerobic training of 12 week duration had any significant effect on the variables listed in the major hypothesis, the data collected were analyzed according to the sub-hypotheses raised for the study.

Sub-hypothesis I

There is no significant effect of aerobic training on serum glucose of overweight Nigerian male adults.

To test this sbub-hypothesis, information regarding the effect aerobic training on serum glucose at baseline, immediately after 6th and 12th week is presented in the descriptive statistical table 4:2.2a.

Table 4:2.2a: Descriptive statistics of means, standard deviation (SD) and standard error of serum glucose of subjects before, during and after 12 weeks of training

Variable	Test period	Means	SD	SEE	% change
Serum Glucose (mg;dl)	Baseline (0week)	102.6	39.65	9.62	
	6^{th} week	96.3	36.09	8.75	6.3 = 6.1%
	12^{th} week	87.8	30.07	7.29	14.8=14.4%

Table 4:2.2a shows the means, SD and SEE of serum glucose of overweight Nigerian male adults at 0 week (baseline), immediately after 6^{th} and 12 week of training. An observation of the baseline data (0 week) showed that the participants had mean serum glucose value of 102.6±39.7mg (2.7mmol/l) the table also revealed that serum glucose mean values after 6^{th} week were 96.3±36.1mg/dl (2.5 mmol/l) and 12^{th} week were 87.8±30.1mg/dl (2.3 mmol/l) of training.

In order to find out whether these decreases were statistically significant, the data were analyzed using repeated measures ANOVA, the result of which is presented in table 4:2.2b.

Table 4:2.2b: Repeated Measures Analysis of Variance (ANOVA) for differences in serum glucose before, during and after 12 weeks of training

Source	SS	DF	MS	F	Sig
Corrected model	1866.39	2	933.20	.74	.48
Intercept	465801.49	1	465801.49	369.79	.00
Training	1866.39	2	933.20	0.79	.48

Error	60462.48	48	1259.63
Total	528130.00	51	
Corrected total	6328.5	50	

F (2,48) = 2.6, P $\geq$ 0.05 * Not significant ** Significant

Table 4:2.2b shows repeated measures ANOVA on serum glucose before, during and after 12 weeks of aerobic training. Observation of the analysis revealed that aerobic training had no significant effect on serum glucose. However, a comparison of baseline and 12th week values showed significant effect of the intercept (P. 000). The null hypothesis was retained.

Sub-hypothesis II

There is no significant effect of aerobic training on serum insulin of overweight Nigerian male adults

To test this sub-hypothesis, information regarding the effect of aerobic training on serum insulin at baseline, immediately after 6th and 12th week is presented in the descriptive statistical table 4:2.3a

4:2.3a: Descriptive statistics of Means, SD and SEE of the subjects on serum insulin before, during and after 12 weeks of training

Variable	Test period	Means	SD	SEE	% change
Serum	Baseline (0wk)	17.4	2.43	0.59	
Insulin	6th week	16.3	6.40	1.55	1.1 = 6.1%
(µm/ml)	12th week	13.3	2.15	0.52	4.1=23.3%

Table 4:2.3a shows the means, SD and SEE of serum insulin of overweight Nigerian male adults at 0 week (baseline), immediately after 6th and 12 week of training. An observation of the baseline data (0 week) showed that the participants had mean insulin value of 17.4±2.4µm. Further observation of the table also revealed means serum insulin of 16.3±6.40µm and 13.34±2.2µm after 6th and 12th week of training respectively.

In order to find out whether these decreases were statistically significant, the data were analyzed using repeated measures ANOVA, the result of which is presented in table 4:2:3b.

Table 4:2:3b: Repeated measures ANOVA for differences in serum insulin before during and after 12 weeks of training

Source	SS	DF	MS	F	Sig
Corrected model	150.37	2	75.18	4.39	.02
Intercept	12558.43	1	12558.43	732.49	.00
Training	150.37	2	75.18	4.39	.02
Error	822.95	48	17.15		
Total	13531.75	51			
Corrected total	923.32	50			

F (2, 48) = 2.6, P≤ 0.05 ** Significant

Table 4:2.3b shows the result of repeated measures ANOVA on serum insulin of the subjects used in this study. The result revealed statistical difference (P = 0.000) after 6th and after 12th week of aerobic training on serum insulin of overweight Nigerian male adults (P < 0.05). The hypothesis of no significant difference was thereby rejected.

To establish which phase of training was responsible for the significant difference, Post-hoc Scheffe's test was applied on the means at baseline, 6th and 12th week and the result is shown in Table 4:2.3c.

Table 4:2.3c: Post Hoc Scheffe's test on the means of insulin before, during and after 12 weeks of training.

(I) TRAINING	(J) TRAINING	Mean Difference (I-J)	Std. Error	Sig.
(Week 0) baseline	week 6 (exercise 1)	1.052941	1.4202249	.761
	WEEK 12	4.052941**	1.4202249	.023
Week 6 (exercise 1)	WEEK 12	3.000000	1.4202249	.118

Significant at baseline and 12th week

Table 4:2.3c shows that the significant difference in the means of serum insulin was due to the mean difference between baseline and 12th week of training (sig .023) $P < 0.05$

Sub-hypothesis III

There is no significant effect of aerobic training on serum glucagon of overweight Nigerian male adults

To test this sub-hypothesis, information regarding the effect of aerobic training on serum glucagon at baseline, immediately after 6th and 12th week is presented in the descriptive statistic in table 4.2.4a

Table 4:2.4a: Descriptive statistics of means, SD and SEE of the subjects on serum glucagon before, during and after 12 weeks of training

Variable	Test period	Means	SD	SEE	% change
Serum	Baseline (0wk)	71.18	5.19	1.26	
Glucagon (pg/ml)	6th week	78.47	3.46	.84	7.3 =10.2%
	12th week	86.23pg	3.59	.87	15.1=21.1%

Table 4:2.4a shows information regarding the descriptive statistics of means, SD and SEE of glucagon at baseline, immediately after 6th and 12th week of training. An observation of baseline (0 week) showed that the participants had mean serum glucagon value of 71.1824 ±5.19 pg/ml. Further observation of the table also revealed mean serum glucagon values of 78.47 ± 3.5pg/ml and 86.2 ±3.6pg/ml after 6th and 12th week respectively.

In order to find out whether these increases were statistically significant, the data were analyzed using repeated measures ANOVA, the result of which is presented in table 4:2.4a

Table 4:2.4b: Repeated measures analysis of variance (ANOVA) for differences in serum glucagon before, during and after 12 weeks of training.

Source	SS	DF	MS	F	Sig
Corrected model	1925.15	2	962.57	58.72	.00
Intercept	315296.09	1	315296.08	1850.80	.00
Training	1925.15	2	962.57	55.72	.00
Error	829.24	48	17.28		

Total	21850.46	51
Corrected total	2754.38	50

F (2,48) = 2.6, P≤ 0.05 ** Significant

Table 4:2.4b shows the results of repeated measures ANOVA on serum glucagon at baseline, 6th and 12th week of aerobic training. The result revealed statistical significant effect of aerobic training after 6th and 12th week of aerobic training (P.000).The hypothesis of no significant difference was hereby rejected.

To establish which phase of training was responsible for the significant difference between the means in the 3 phases of data collected, post-hoc scheffe's test was applied on the means at baseline, after 6th and 12th week of training, the results which are shown in table 4:2.4c.

Table 4:2.4c. Post hoc scheffe's test on the means of glucagon before, during and after 12 weeks of training.

(I) TRAINING	(J) TRAINING	Mean Difference (I-J)	Std. Error	Sig.
0 week baseline	week 6	-7.288235**	1.4256365	.000
	WEEK 12	-15.047059**	1.4256365	.000
week 6	WEEK 12	-7.758824**	1.4256365	.000

** Significant

Baseline vs 6th week, Baseline vs 12th week and 6th week vs 12th

Table 4:2.4c showed that the significant difference in the means of serum glucagon in the phases of training was due to the mean difference between baseline vs 6th week, baseline vs 12th week, and 6th week vs 12th week.

Sub-hypothesis IV

There is no significant effect of aerobic training on serum triglycerides of overweight Nigerian male adults.

To test this sub-hypothesis, information regarding the effect of aerobic training on serum triglycerides before, during and after training is presented in descriptive statistical table 4:2.5a.

Table 4:2.5a: Descriptive statistics of means, SD and SEE of subjects on triglycerides (TG) before during and after 12 weeks of training.

Variable	Test period	Means	SD	SEE	% change
Serum Triglycerides (mg/dl)	Baseline (0wk)	128.47	34.02	8.25	
	6th week	110.94	30.97	7.51	17.5mg/dl=13.7%
	12th week	96.41	26.94	6.53	32.1mg/dl=24.9%

Table 4:2.5a shows the Means, SD and SEE of the serum triglycerides at baseline, immediately after 6th and 12 week of aerobic training of overweight Nigerian male adults. An observation of baseline data (0 week) showed that the participants had serum TG values of 128.5 ±34.02mg/dl (3.3mmol/l). Further observation of the table also revealed means TG values of 110.9± 30.97 (2.9mmol/l) and 96.4 ±26.9 (2.5mmol/l) after 6th and 12th week respectively.

In order to find out whether these decreases were statistically significant, the data were analyzed using repeated measures ANOVA, the result of which is presented in table 4:2.5b.

Table 4:2.5b: Repeated measures analysis of variance for differences in serum triglycerides before, during and after 12 weeks of training.

Source	SS	DF	MS	F	Sig
Corrected model	8761.53	2	4380.77	5.63	.015
Intercept	639072.18	1	639072.18	674.64	.000
Training	8761.53	2	4380.77	4.63	.015
Error	45469.29	48	947.28		
Total	693303.00	51			
Corrected total	54230.82	50			

F (2, 48) =2.6, P ≤ 0.05** Significant

Table 4:2.5b shows the results of repeated measures ANOVA on serum TG of the participants used in this study. The result revealed statistical significance after 6th and 12th week of aerobic training on serum TG of overweight Nigerian male adults ($P < 0.05$). The null hypothesis of no significant difference was rejected.

To establish which phase of training was responsible for the significant difference between the means, post hoc Scheffe's test was applied on the means at baseline, after 6th and 12th week, results of which are shown in table 4.2.5c.

Table 4:2.5c: Post hoc scheffe's test on the means of triglycerides before, during and after 12 weeks of training

(I) TRAINING	(J) TRAINING	Mean Difference (I-J)	Std. Error	Sig.
Week 0 baseline	week 6	17.53	10.56	.26
	WEEK 12	32.06**	10.56	.02
Week 6	WEEK 12	14.53	10.56	.40

Baseline vs 12th week ** Significant

Table 4:2.5c shows that, the significant difference in the means of serum triglycerides was due to the mean difference of baseline Vs 12th week (sig .015) less than P.> 0.05.,

Sub-hypothesis V

There is no significant effect of aerobic training on serum cholesterol of overweight Nigerian male adults.

To test the sub-hypothesis, information regarding the effect of aerobic training on serum Cholesterol (TC) before, during and after training is presented in the descriptive statistical table 4:2.6a

Table 4:2.6a. Descriptive statistics of Means, SD and SEE of subjects on serum Cholesterol (TC) before, during and after 12 weeks of training

Variable	Period of training	Mean	SD	SEE	% Change
Serum Cholesterol (mg/dl)	Baseline 0week	200.46	32.18	7.81	
	6^{th} week	190.2l	27.27	6.62	10.2 = 5.1%
	12^{th} week	173.98	23.34	5.66	26.5=13.2%

Table 4:2.6a shows the Means, SD and SEE of the serum TC at baseline, immediately after 6^{th} and 12^{th} week of aerobic training of overweight Nigerian male adults. An observation of the baseline data showed that the participants had mean TC value of 200.5 $\pm$32.2 mg/dl (5.2mmol/l). Further observation of the table also revealed that the means serum TC were 190.27 $\pm$27.3mg/dl (4.95mmol/l) and 17.98 $\pm$23.3 mg/dl (4.95mmol/l) after 6^{th} and 12^{th} week respectively.

.In order to find out whether these decreases were statistically significant, data were analyzed using repeated measures ANOVA, the results of which are shown in table 4: 2. 6b.

Table 4:2.6b: Repeated measures analysis of variance (ANOVA) for difference in serum cholesterol. (TC) before, during and after 12 weeks of training

Source	SS	DF	MS	F	Sig
Corrected model	6063.958	2	3031.98	3.91	.027
Intercept	1807096.471	1	1807096.47	2330.41	.000
Training	6063.958	2	3031.98	3.91	.027
Error	37221.161	48	776.44		
Total	1850381.590	51			
Corrected total	43285.119	50			

F (2,48) = 2.6, P$\leq$ 0.05 ** Significant

Table 4.2.6b, shows that result of repeated measures ANOVA on serum TC of the participants used in this study. The result revealed statistical significance effect after 6th and 12th week of moderate intensity aerobic training on serum TC of overweight Nigerian male adults (P < 0.05). The null hypothesis of no significant difference was rejected.

To establish the phase of training that was responsible for the significant difference, post-hoc scheffe's test was applied on the means at baseline, 6th and 12th week, the result of which is presented in Table 4:2.6c.

Table 4:2.6c: Post hostScheffe's test on the means of cholesterol before, during and after 12 weeks of training.

(I) TRAINING	(J) TRAINING	Mean Difference (I-J)	Std. Error	Sig.
week0	week 6	10.188235	9.5513526	.570
baseline	WEEK 12	26.476471**	9.5513526	.028
Week 6	WEEK 12	16.288235	9.5513526	.244

Baseline vs 12th week ** significant.

Table 4:2.6c shows that the significant difference in the means of cholesterol was due to the mean difference of baseline Vs 12th week (sig. 028), less than P > 0.05.

Sub-hypothesis VI

There is no significant effect of aerobic training on serum high density lipoproteins level of overweight Nigerian male adults

To test this sub-hypothesis, Information regarding the effect of aerobic training on serum high density lipoproteins (HDL) levels before, during and after training is presented in the descriptive statistical table 4:2.7a

Table 4:2.7a: Descriptive statistics of Means, SD and SEE of subjects on serum high density lipoproteins (HDL) before, during and after 12 weeks of training.

Variable	Period of training	Mean	SD	SEE	% Change
	Baseline 0week	53.48	14.04	3.41	
Serum	6^{th} week	54.31	11.27	2.73	.08 =1.5%
HDL (mg/dl)	12^{th} week	54.74	6.99	1.70	1.3 =2.3%

Table 4:2.7a shows the means, SD and SEE of the serum HDL at baseline, immediately after 6^{th} and 12^{th} week of aerobic training of overweight Nigerian male adults. An observation of baseline data showed that the participants had mean HDL value of 53.5 $\pm$ 14.04mg/dl (1.4mmol/l). Observation of the table revealed that the means serum HDL were 54.31 $\pm$ 11.3mg/dl (1.41mmol/l) and 54.7 $\pm$ 6.99 mg/dl (1.4mmol/l) after 6^{th} and 12^{th} week respectively.

In order to find out whether these decreases were statistically significant, the data were analyzed using repeated measures ANOVA, the result of which is presented in table 4: 2.7b.

Table 4:2.7b Repeated measures analysis of variance (ANOVA) for differences in serum HDL before, during and after 12 weeks of training.

Source	SS	DF	MS	F	Sig
Corrected model	13.78	2	6.89	.06	.946
Intercept	149678.75	1	149678.75	1204.25	.000
Training	13.784	2	6.89	.06	.946
Error	5966.01	48	124.29		
Total	155668.55	51			
Corrected total	5979.80	50			

F (2, 48) = 2.6, P< 0.05 * * Significant, *Not Significant

,

Table 4:2.7b shows the results of repeated measures of ANOVA on serum HDL before after 12 weeks of aerobic training. An observation of the analysis revealed that the training had no statistical effect on serum HDL. However, a comparison of baseline and 12th week values showed significant effect on the intercept (P.000). The null hypothesis was only retained as pre-posttests.

Sub-hypothesis VII

There is no significant effect of aerobic training on serum low density lipoproteins (LDL) of overweight Nigerian male adults

To test the sub-hypothesis on low density lipoproteins, information regarding the effect of aerobic training on serum LDL before, during and after training is presented in the descriptive statistical table 4:2.8a.

Table 4:2.8a: Descriptive statistics of Mean, SD and SEE of subjects on low density lipoproteins (LDL) before, during and after 12 weeks of training.

Variable	Period of training	Mean	SD	SEE	% Change
Serum	Baseline 0week	117.87	34.81	8.44	
LDL	6th week	115.80	23.21	5.63	2.1 =1.8%
(mg/dl)	12th week	98.81	19.99	4.85	19.1=16.2%

Table 4:2.8a shows the means, SD and SEE of the serum LDL at baseline, immediately after 6th and 12th week of aerobic training of overweight Nigerian male adults. An observation of baseline data showed that the participants had mean LDL values of 117.9 ±34.8mg/dl (3.1mmol/l). Further observation of the table also revealed that mean serum LDL were 115.80 ±23.2mg/dl (3.01mmol/l) and 98.8 ±19.99 mg/dl (2.6mmol/l) after 6th and 12th week of training respectively.

In order to find out whether these decreases were statistically significant, the data were analyzed using repeated measures ANOVA, the result of which is shown in table 4.2.9b.

Table 4:2.8b: Repeated measures analysis of variance (ANOVA) for differences in the serum LDL before, during and after 12 weeks of training.

Source	SS	DF	MS	F	Sig
Corrected Model	3716.64	2	1858.32	2.59	.085
Intercept	626.64	1	628396.75	874.04	.000
Training	626396.75	2	1858.32	2.59	.085
Error	3716.6	48	716.67		
Total	34400.26	51			
Corrected total	664513.65	50			

F (2, 48) = 2.6, P ≥ 0.05 = Significant

Table 4.2.8b showed repeated ANOVA on serum LDL before during and after 12 weeks of aerobic training. An observation of the analysis revealed that the training had no statistical significant effect on serum LDL. However, a comparison of baseline and 1212th week values showed significant effect on intercept (P.000). The null hypothesis was only retained as pre-posttests.

Discussion

The purpose of this study was to investigate the effects of 12 weeks aerobic training on serum glucose, insulin, glucagon lipids and lipoproteins of overweight Nigerian male adults. For the purpose of this study, seventeen (17) male adults of mean age 34.1years, mean height 1.65m, mean weight 72.8 kg and mean BMI 26.8 kg/m^2 at baseline were judged to meet the criteria for overweight male adults required for the study.

Studies (Wilmore, 1983; Jonas, 2001) have shown that a reduction in body weight alters the body mass index of an individual. Available evidence has shown that aerobic training significantly reduces body weight, although, at gradual pace (Baumgertner et al; 2006; Plowman & Smith, 2008). The result of this study revealed that weight/BMI of participants was reduced by 2.2kg and 1.0kg/m^2 respectively after 12 weeks of aerobic training. The result of the study showed significant reduction in body weight/BMI after 12 weeks of aerobic training. Although, the decrease in body weight/BMI was significant, substantial weight loss can only be achieved when a negative caloric balance is achieved (Wilmore, 1983). In contrast to the result of this study, Coker et al; (2006) examined the influence of moderate intensity exercise training versus insulin stimulated in adults and reported no change in body weight or fats. This supports the assertion that body weight is not lost faster unless exercise is combined with caloric restrictions (Jonas, 2001).

It is apparent that any physical stress imposed on the body that requires an increase in muscle metabolic and atleast subsequent utilization of blood glucose obligatorily requires strict glucose regulatory mechanism (Coker & Kjaer, 2005; Godwin, 2010). Physical traning has been reported to lower blood glucose level (Colberg & Greico, 2009). In contrast, the result of this study did not show significant decrease in the means of serum glucose after 12 weeks of aerobic training. The baseline values indicated that subjects for this study fall within the borderline for mild hyperglycemia (Plowman & Smith, 2008; Powers & Howley, 2012). Although the decrease was not significantly differencwithin the training period, a mean decrease of 14.8 mg/dl (14.4%) was achieved as training effects after 12 weeks

of training. As the increase demand for glucose was met by increasing hepatic glucose production by two to three folds with concomitant increase in plasma level of glucagon (Galbo et al; 1977; Pierce, 1999; Sato 2000; Sigal et al; 2006; Krishna et al; 2013), and other related hormones like growth hormones, catecholamine and cortisol (Bent, 1986; Roy & Parker, 2007; Plowman & Smith, 2008; Powers & Howley, 2012), the elevated muscle glucose uptake rate has been reported to gradually decline to the basal level during the recovery period. During the postexercise recovery period, lactate consumption by the liver increased significantly serving as a substrate for accelerated postexercise gluconeogenesis (Roy & Parker, 2010). It is believed that the non-significant decrease in glucose levels in this study is attributed to the elevated gluconeogenesis to replete the liver stores and restore normoglycemia after training. The training intensity was also assumed to be high and had affected the outcome of the study, as studies (Anderson et al; 1982; Wolfe et al; 1985; Roy & Parker, 2007), have reported that strenuous exercise increase glucose level. In view of the importance of glucose kinetics during exercise and the hormones responsible for glucose homeostasis, several studies (Cogan et al; 1995; Pierce, 1999; Bergman et al; 2000; Sigal et al; 2006), have addressed the effect of exercise on glucose kinetics. Similarly, Costil et al; (1973), reported a slight increase in serum glucose of 6mg/dl after 30 minutes of exercise and no further increase during rest. Naveri et al; (1978), reported 71% increase immediately after strenuous training. Anderson et al; (1982), reported an increase of 200mg/dl immediately after exercise. The increase was attributed to as normal response and not related to impaired glucose tolerance or inability to utilize glucose efficiently.` The non significant decrease in blood glucose was as a result of hormonal adaptation that insured increased hepatic glucose utilization rate of exercising muscles (Hu & Manson, 2003; Sigal et al; 2006; ACSM et al; 2009). This increase suppressed the role of insulin activated the and activities of glucagon (gluconeogensis and glycogenolysis) in the elevation of glucose (Landt et al; 1985; Goodwin, 2010). The results of this study is similar to the findings of Von der Heijden et al; (2009), when they determined whether a controlled aerobic exercise programme improves peripheral and hepatic insulin sensitivity and affects glucose production rate (gluconeogensis and glycogenolysis) in sedentary lean and obese Hispanic adolescents.

They reported that glucose production rate decreased slightly 3±1% (lean) (P< .05) and 4±1% (obese) (P<0.01). With hormonal control, plasma glucose homeostasis was maintained during exercise because the increase in glucose uptake was balanced by a corresponding increase in glucose production (Wolfe, 1985).The non significant decrease in serum glucose level in this study explains the assertion by America Diabetic Association (2001), that hypoglycemia during physical activity rarely occurs in non-diabetic individuals. Contrary to these findings, Transey et al; (20o6), examine the acute glucose-lowering effects of aerobic exercise and reported that plasma glucose dropped by 25% from baseline. Roy & parker, (2007), also reported that during prolonged exercise, glucose levels dropped significantly. The mechanism responsible for the non significant decrease of glucose level in this study is difficult to explained base on the conflicting results reported by the various conclusions. It is apparent that any physical stress imposed on the body that requires an increase in muscle metabolism and atleast substantial utilization of blood glucose obligatorily requires strict glucose regulatory mechanism (Coker et al; 2006}

During aerobic exercise, the serum insulin concentration normally falls with a rise in plasma glucagon (Landry 2002; Khoo et al; 2010). Insulin and glucagon are implicated in tissue metabolism of blood levels of glucose, fatty acid, triglycerides and amino acids (Kang et al; 1996; Ganong, 2001). The results of the study showed a significant suppression/decrease (P<0.05) in the serum insulin levels after 12 weeks of aerobic training. A decrease of 4.1 (23.30%) μ/ml of insulin was achieved by the end of 12 weeks training. The decrease in insulin level in this study replicates the positive influence of aerobic exercise training as reported in numerous investigations. Wolfe et al; (1986), in a simulation study of mild exercises for 60 minutes to evaluate the physiological effects of exercise on plasma insulin concentration, reported a decline from basal level (12.2μm/ml) with the onset to the end of exercise. Zalie et al; (2001), reported that 10 weeks of physical activity intervention significantly decreased fasting insulin in young adults. Nashida et al; (2010), reported that after aerobic training, fasting insulin levels decreased by 13%. Although results of this study indicated a 23.2% decrease above the values

reported by Nashida et al; (2010), the result of this study supports their conclusion that during light to moderate exercise, a reduction in insulin concentration is to maintain plasma glucose homeostasis. Since insulin and glucagon are responsible for glucose homeostasis, the minute to minute regulation of body's integrated metabolism and stabilizing the body's melieu, insulin decrease in this study is of course an appropriate response to the 12 weeks training.

The result of the study showed significant increase in the serum glucagon levels after 12 weeks of aerobic training. The result indicated that the increase was 7.3pg/ml (10.2%) and 15.1pg/ml (21.1% by the end of 6^{th} week and 12^{th} week of training respectively. Studies have shown that during prolonged exercise, the main stimulus that promotes an increase in glucagon secretion from pancreases is a drop in plasma glucose concentration and concomitant drop in insulin (Landry 2002; Dunning et al; 2005, Williams, 2007). Exercise has been reported to be a unique model for studying glucagon action because it allows for an increase in glucagon to be studied without creating hyperglycemia or hyperinsulinemia (Aburand et al; 1989). Krishna et al; (2013), in their study to determine the role of glucagon on hepatic glutamine mobilization during exercise, revealed that plasma glucagon concentration rose two-fold on the course of the exercise period. Anderson et al; (1982), studied the effect of exercise or serum glucose, insulin, glucagon and chromium excretion, and reported that serum glucagon immediately after running was significantly elevated compared with the observed prior to 2 hours after running. Khoo et al; (2010), similarly reported a rise in glucagon level at rest after training ($P< 0.01$). The 18.5 % rise of glucagon after 12 weeks moderate intensity aerobic training in this study fall in line with the findings reported above.

Many types of exercise appear to positively influence blood lipid profiles. Such changes in lipid profiles related to exercise training include reduction in triglyceride levels (Leon & Sanchez, 2001; Durstine et al; 2002). Philip et al; (1996), and Romijn et al; (1993), demonstrated that intense and long term exercise increase lipids kinetics. The result of this study showed significant decrease in

triglycerides (TG) by the end of 12 weeks period of aerobic training ($P < 0.05$). The result of this study showed that decrease of 17.5mg/dl (o.5mmol/l) (13.7%) and 32.1mg/dl (0.8mmol/l) (24.96%) were achieved as training effects after 6th and 12th week of aerobic training The result of this study supports the findings reported by Mohammed (2003), that a TG basal value of 3.15 dropped to1.50±12 after 12 weeks training when he studied the physiological variables of non-insulin dependent diabetes using bench step as a mode of exercise. Using the meta-analytic approach to examine the effects of aerobic exercise on lipids and lipoproteins in overweight adults, Kelley et al; (2005), reported 11% (7.3mg/dl) improvement in TG, and concluded that aerobic exercise decreased TG in overweight and obese adults. Dustine et al; (2001), in a meta-analysis of well controlled study, indicated that exercise volume of 1200-2200 calories per week lowered TG levels by 5.038 mg/dl. Habibzadeh, (2010), reported that TG significantly decreased ($P<0.05$) in a 2 month walking exercise in young obese women. Similarly, Guo et al; (2011), reported significant improvement in TG at the end of the three months aerobic exercise training on lipids profiles in Japanese workers. The result of this study supports the conclusions drawn by the studies cited above.

Several studies have i0ndicated that cholesterol levels can be reduced through exercise training. Such positive changes include reduction in TG/LDL-C levels, raised HDL-C levels and reduced TG levels (Thomas et al; 2004; Wayo, Gwani, Chado & Haruna, 2012). The result of this study showed significant decrease in serum cholesterol after 12 weeks of aerobic training ($P<.05$). A decrease of 10.2 mg/dl (0.3mmol/l) (5.1%) and 26.5(0.3mmol/l) (13. 2%) mg/dl was achieved as training effects after 6th and 12 week of aerobic training. The result of this study is in line with studies that have shown that cholesterol levels decrease due to exercise training. Tolfrey et al; (2000), reported that trained or active youths showed favorable levels of total cholesterol. Kelley et al; (2005) reported that across all categories (340 exercise, 265 control), random effect modeling resulted in statistical improvement in serum cholesterol.

Regular endurance exercise is widely recognized modality to raise plasma HDL-C level (Despress, 1994), which is one of the metabolic adaptations contributing to the reduced risks of coronary heart diseases (CHD) observed among physically active and fit individuals (Blair et al; 1997). Moderate jogging and brisk walking for about 30 minutes, 3-5 times a week, is necessary to produce improvement in HDL-C (Venkarteswarlu, 2010). The results of this study did not show significant different as a result of the 12 weeks aerobic training on serum HDL-C (P> 0.05). A slight increase of 1.3mg/dl (0.03mmol/l) (2.34%) was recorded as effects of the 12 weeks aerobic training. This increase in HDL-C is of substantial importance in public health (Kodama et al; 2007). This elevation in HDL-C demonstrated by this study is of clinical importance which is not far from the findings of previous studies wherein Kelley et al; (2004), and kodama et al; (2007), reported mean net elevation in HDL-C level of 1.2mg/dl (0.03mmol/l) and 1.9mg/dl (0.05mmol/l) respectively. Aerobic exercise is believed to reduce the risk of cardiovascular diseases partially through increasing serum level of HDL-C, however, this effect varies considerably among exercise intervention studies. Kodama et al; (2007), used electronic database searches for randomized controlled trials that examined the effect of exercise training on HDL-C level. They reported that mean net change in HDL-C level was statistically significant but modest (2.53mg/dl[0.065mmol/l] p.001). Although, low HDL-C concentration is often accompanied by an elevated TG level associated with abdominal obesity and an insulin resistance –hyperinsulinemia state (Despress, 1994), some individuals are characterized by low HDL-C level without obesity or hypertriglyceridemia or a condition called hypoalphalipoproteinemia (lavie et al; 1992; Goldbourt et al; 1997). Since studied have shown that the positive effects of exercise training include raised HDL-C (Leon Sanchez, 2001), the result of this study supports the report by Thompson et al; (2001), who observed that exercise increases HDI-C, and Blessing et al; (1999), who observed positive effect in HDL-C, TC/HDL-C levels after a 12 week training program involving young adults of 13-18 years. Similarly, Durstine et al; (2001), in a meta-analysis of well controlled study, concluded that an exercise of volume of 1200-2200 calories per week is effective at elevating HDL-C levels from 2-08 mg/dl and lowering TG levels by 5-3.8 mg/dl. Adeyanju (2002), observed a significant sex specific increase in HDL-C (F-34.54 P< 0.05), as effects of continuous and

interval training. Kelley et al; (2005), reported 3% changes in HDL and 2% changes in TC as equivalent to improvement. Guo et al; (2011), reported a significant improvement in HDL-C at the end of three months aerobic training. Similarly, Jatau et al,; (2012), reported considerable increase in HDL-C in experimental group from 29.4±6.84 mg/dl before start of training to 42.39±6.5 mg/dl after training. These studies have shown that aerobic exercise training modestly increased HDL-C. in contrast to some of the studies cited above, the result of this study did not show significant effect of 12 weeks aerobic training on HDL-C The result of this study falls in line with the findings and conclusions drawn above. However, at the minimum level of exercise, changes in HDL-C and TG are sometimes small and unpredictable, but exercise program of longer duration 45 minutes or longer higher intensity and more frequency, produce much more effects on HDL-C and TG. Experts (Wilmore & Costill, 2004; Plowman & Smith, 2008), reported that activities of high intensity produce significant effect on HDL-C when compared with those of low intensity as shown in this study.

The results of this study did not show any significant decrease in LDL as a result of the 12 weeks aerobic training (P 0.05). As a result of the 12 weeks aerobic training, baseline values of 117.9mg/dl (3.1mmol/l) dropped by 2.1mg/dl (0.1mmol/l) (1.75%) after 6 weeks, and 19.1mg/dl (0.5mmol/l) (19.17%) after 12 weeks of training. The training intensity used for this study was considered to be too low to produce significant effect on HDL-C of overweight adults (Wilmore & Constil, 2004; McArdle et al; 2010). Many types of exercise training appear to positively influence lipid profiles metabolism. Thompson et al; (2001), reported that positive changes related to exercise training include reduction in LDL-C level. Mohammed (2003), assessed the effects of aerobic exercise on selected physiological variables and reported a significant difference in LDL-C (± 6.38). Adeyanju (2002) observed significant effects of training on LDL-C by training group LDL-C (F.29, 751, 4.05). In a similar manner, Kelley et al; (2005), observed a 3% change in LDL-C which was equivalent to improvement from a meta-analytic approach to examine the effects of aerobic exercise on lipids and lipoproteins in overweight and obese adults. The decrease observed in this study is a positive effect related to training.. This study is in line

with the findings reported by Jatau et al; (2012), that 12 weeks aerobic training did not significantly decrease LDL-C in the experimental group after 12 weeks training. They reported that the non non significant decrease in LDL-C was attributed to low intensity aerobic training level used in this study as against high intensity training reported by Wilmore & Costill, (2004).

Implications of the Study

Clinical epidemiological and basic research evidence clearly support the inclusion of regular physical activity as a tool for the prevention of chronic diseases and the enhancement of overall health (Williams, 2007; Plowman & Smith, 2008). An impressive body of epidemiological evidence suggests that overweight is a risk factor for later development of health complications of hyperglycemia (T2D), insulin resistane, aberrant lipids and lipoproteins metabolism. A decrease in body weight/BMI of 0.5kg/m^2 due to exercise training has been considered as positive exercise training effect (Dullo, 2005; Williams, 2007). The decrease in BMI of 0.8kg/m^2, 14.8mg/dl (0.2mmol/l), of glucose, 4.1µm/ml of insulin, 32.1mg/dl (0.9mmol/l) of triglycerides, 26.5mg/dl (0.7mmol/l) of cholesterol, and the increase of 1.3mg/dl (0.03mmol/l) and 19.1mg/dl (0.5mmol/l), reported in this study have positive health effects on overweight adults. The health implications as reported by Tansy et al; (2006), for glucose; van der Heijden et al; (2009), for insulin sensitivity; Nishida et al; (2010), for glucagon; Habibzadeh, (2010), for triglycerides and cholesterol; Kelley et al; (2004); Kodama (2007), for high density lipoproteins and low density lipoproteins respectively, are modest decreases and increases that have positive clinical importance on the health of the overweight adult. The overweight adult who walks and jogs three times a week for thirty minutes will achieve greater physiological benefits, delay the onset of obesity and prevent the health complications associated with overweight. By implication, Thompson, (2001), noted that acute exercise are of significant importance and can lead to clinical meaningful improvement in the control of metabolic syndromes even in the absence of weight loss.

CHAPTER FIVE

5.0 SUMMARY, CONCLUSION AND RECOMMENDATIONS

This chapter presents the summary, conclusion of the findings of the effect of aerobic training on serum glucose, insulin, glucagon, lipids and lipoproteins of overweight Nigerian male adults. Recommendations on the use of aerobic training to reduce the onset of type 2 diabetes are made.

5.1 Summary

This study was conducted to find out the effect of aerobic training on serum glucose, insulin glucagon lipids and lipoproteins of overweight Nigerian male adults. To achieve this purpose, 17 subjects from ECWA College of Health Technology, Kagoro, who met the inclusion criteria based on their BMI, were selected for the study. On their willingness to undergo 12 weeks aerobic training, baseline data including age, height, weight, and blood samples (under strict antiseptic conditions) were taken for the estimation of serum glucose, insulin, glucagon, triglycerides, cholesterol, high density lipoproteins and low density lipoproteins at the Chemical Pathology Department, Ahmadu Bello University Teaching Hospital, Zaria

Training commenced after all baseline samples were taken. The training consisted of walking and jogging for 30 minutes on 3 alternate days a week in the first 3 weeks; 40 minutes in the 4^{th} -6^{th} week, 45 minutes in the 7^{th} -9^{th} week and 50 minutes in the 10^{th}- 12 week at <40 -60% HR max of the subjects. Increase in duration after 3 weeks of training was due to subjects' adaptation to training. The workload commenced from very light to moderate, i.e. from <40 -60% HR max of aerobic training throughout the period of training. Weight of subjects and blood samples were further taken after 6^{th} and 12^{th} week of training to test for fasting blood sugar, insulin, glucagon, triglycerides, cholesterol, HDL-C and LDL-C.

The data collected were statistically analyzed using descriptive and repeated measures analysis of variance (ANOVA).

The result of this study showed that:

I Aerobic training did not produce significant decrease in serum glucose of overweight Nigerian adults.

2) Aerobic training produced significant decrease in serum insulin of overweight adults

3) Aerobic training produced significant increase in serum glucagon of overweight Nigerian male adults.

4) Aerobic training produced significant decrease in both triglycerides and cholesterol of overweight Nigerian male adults.

5) Aerobic training did not produce significant increase in HDL-C and significant decrease in LDL-C of overweight Nigerian male adults

5.2 Conclusion

Regular aerobic training performed on 3 alternate days at intensity levels of 40-60% HR max for training session lasting between 30 and 50 minutes for 12 weeks:

1. Reduced serum glucose in overweight Nigerian male adults between the ages of 25-35 years, although, not statistically significant (P >.05)

2. Reduced serum insulin a in overweight Nigerian male adults between the ages of 25 and 35, years (P< 0.05).

3. Increased serum glucagon in overweight Nigerian male adults between the ages of 25 and 35 years (P< 0.05).

4. Reduced serum lipids (TG & TC) levels of overweight Nigerian male adults between the ages of 25 and 35 years ($P< 0.05$).

5. Did not significantly increase HDL-C and reduce LDL-C of overweight Nigerian male adults between the ages of 25 and 35 years ($P> 0.05$).

5.3 Recommendations.

On the basis of the findings of this study, the following recommendations were made.

1. Moderate walking and jogging has been shown to decrease serum glucose, therefore, for overweight Nigerian male adults to overcome the onset of lifestyle related diseases, walking and jogging should be undertaken regularly.

2. Since walking/jogging was found to improve the hormonal regulatory role of insulin and glucagon on glucose utilization, it was suggested that health professionals and fitness centers should use this method of training on overweight adults to reduce insulin resistance, impaired glucose transport and improve insulin sensitivity.

3. Aberrant lipids metabolism is implicated in the cause of T2DM and hypertension. Exercise scientists and fitness providers should use walking/jogging on their clients to regulate lipids concentration in overweight adults.

4. In view of the beneficial role of exercise training for health in the overweight, overweight adults should personally engage in regular walking/jogging as a prophylactic measure against obesity and its associated health problems.

5.4 Recommendation for Further Studies

The researcher identified some related problematic areas in the course of this study that will need further investigation.

1. The result of the study showed that serum insulin was suppressed and an accelerated rise in serum glucagon after 6 weeks of training in overweight adults. It is not clear whether the rise will continue in such a sharp rise if training continued after 12 weeks in diabetics. It is therefore suggested that an investigation be conducted to investigate the consistency of the regulatory role of metabolic hormones in diabetic patients.
2. Studies have shown that significant decrease in triglyceride and cholesterol significantly lead to elevated HDL and decreased LDL. As this study did not show any significant effects on HDL-C and LDL-C, a similar study with a high intensity aerobic training will be appropriate.
3. As this study was conducted on overweight male adults, a similar investigation using the same variables should be conducted on overweight/obese female adults.

REFERENCES

Abbasi, F., Brown, B.W.B., Lamendola, C., McLaughlin, T. & Reavens, G.M. (2002). Relationship between obesity, insulin resistance, and coronary heart disease risk. *Journal of American College of Cardiology, 40,s 937-943.*

Abbasi, F., M.C., Laughlin, T., Lamedola, C., Kim, H.S., & Tanaka, A., (2000). High carbohydrate diets, triglyceride-rich lipoprotein, nd coronary heart disease risk *America Journal of Cardiology, 85, 45-48.*

Abbasi, F., McLaughline, T., Lamendola, C. & Reavens, G.M., (2006).The relationship between glucose disposal in response to physiological hyperinsulinemia, and basal glucose and free fatty acid concentration in the healthy volunteers. *Journal of Clinical Endocrinology and Metabolism, 85; 1251-1254*

Abumrad N.N., Williams P.E., Frexes-Steed, M; Geer, R., Fla Koll, P., Cersosimo, E., Brown, L.L., Melko, I., Bulus, N., Hourani, H., Hubbard, M., & Glrushan, F. (1989). Inter organ Metabolism amino acids in vivo. *Diabetes Metabolism Review* 5,213-226.

Achten, J. & Jeukendrup, N., (2004). Optimizing fat oxidation through exercise and diet. *Nutrition 20*, *716-727*.

Adeyanju, E.S. (2002). Comparative effects of continuous and interval training on body composition and lipoprotein profiles of male and female adolescent in Nigeria. Unpublished Ph.D dissertation, Ahmadu Bello University, Zaria, Nigeria.

Ahn, S. (2007). Effects of Walking on Cardioviascular risk factors and psychological outcomes in postmenopausal obese women. School of Nursing Champagn, National University, Korea, 37(4); 519, p. 528.

Albright, A. Franz, M., Hornsby, G., Kriska, A., Ullrich, I., Venty, I.S., American College of Sports Medicine Position Stand, (2000). Exercise and type 2 diabetes. *Medicine & Science in Sports & Exercise, 32 (7): 1345-1360).*

Allain, C.C. Poon, L, Chan, S.G, Richmond, W. & Fu, P. [1974]. Enzymatic determination of total serum cholesterol; *Clinical Chemistry* 20; 470

Al-Mousa, Z. & Parkash, P. (2000). Prevalence of overweight and obesity among Kuwaiti children and adolescents; *Bahrain Medical Bulletin 22, 123-127.*

Al- Sendi, A.M., Shetty, P., Musaiger, A.O. & Myatt, M. (2003). Relationship between body composition and blood pressure in Bahrain adolescents. *British Journal of Nutrition* 90, 837-844.

American Alliance for Physical, Health Education, Recreation, and Dance (AAPHERD), (1990). Life Time Health Related Fitness Tests Manual; *AAPHERD*, *Keston Varania*.

American College of Sports Medicine, Chodzleo-Zoyko, W.J. Proctor D.N. Flatarone-Singh,M.A., Minson, C.T., Nigy, C.R., Salem, G.J., Skinner, J.S., American College of Sport Medicine Position Stand, (2009). Exercise and Phsyical activity for older adults. *Medicine* & *Science* in Sports *& Exercise*, 41(7), 1510-1530.

American College of Sport Medicine, (2000). *Guidelinens for Exercise Testing and Prescription* (*6th ed*); Philadelphia; PA: Lippincott, Williams & Wilkins.

American Diabetes Association, (2003). Exercise and diabetes mellitus. *Diabetes Care*, 26, 575-577.

American Diabetes Association (2005). Slender or medical care for clients with diabetes mellitus. *Diabetes care*, 45 (10), 1289-1298.

American Dietetic Association, (2004). Physical activity/exercise and diabetes. *Diabetes Care*, (*27 Supp*) I, 559-562.

American Dietetic Association, (2008).Roles of the replacers in diabetes medical nutrition therapy. *Diabetes Care*, 23, 596-97.

American Dietetic Association,(2005). Position of the American Dietetic Association: Fat replacers. *Journal of the American Dietetic Association, 105, 266-275.*

American Heart Association,(1996).Dietary Guidelines for Health American Adults. *Circulation, 94, 1795-1800.*

American Heart Association, (1997). Monounsaturated fatty acids and risk of cardiovascular diseases. *Circulation, 1253-1258.*

Anaja, H.P., Isah, H.S., Abdu, Aguye, I. & Oboru, N.A. (1995). Lipids profiles in diabetic Nigerians: Zaria Update. *International Diabetic Digest, 6 (4), 90-93.*

Anderson, R.A., Polasnky, M.M., Bryden, N.A., Roginski, E.E., Patterson, K.Y. & Reamer, D.C. (1982). Effects of exercise (running) on serum glucose, insulin, glucagon, and chromium excretion. *Diabetes, Vol. 31; 212-216*

Anderson, L.B., Harro, M., Sardinha, L.B., Froberg, K., Ekelund, U., Brage, S. & Anderson, S.A. (2006). Physical activity and clustered cardiovascular risk in children: a cross-sectional study. (The European Youth Heart Study), *Lancet*, *368*, *299-304*

Assali, A.R., Ganor,A., Beigel, Y., Shafer, Z. & Hershcovici, T. |(2001). Insulin resistance in obesity: body weight or energy balance, *Journal of Endocrinology, A1, 195-198.*

Bachmann, O.P., Dahldo, M.B. & Brechtol, K. (2001). Effects of intravenous and dietary lipid challenges on vitra myocellular lipid content and the relation with insulin sensitivity in human. *Diabetes, 50, 2579-2584.*

Bajaij, M., Suraamornkul,S., Romanejji, A., Cline, W., Mandarino, L.J., Shulman, G.I., & Defrozo, R.A. (2005). Effect of sustained reduction in plasma free fatty acid concentration on intramular long-chain fatty acid Acetyl-COAs and insulin action in type 2 diabetic patients. *Diabetes, 54,3148-3153.*

Baumgartner, T.A., Jackson, A.S., Mahar, M.T. & Rowe, D.A., (2007). *Measurement for Evaluation in Physical Education and Exercise Science (8th edition);* Boston; McGraw Hill Higher Education.

Bell, L.M., Watts, K., Sinfarikas, A., Thompson, A., Ratnam, N., Bulsara, M., Finn, J., O'Doiscoll, G., Green, D.S., Janes, T.W. & Davis E.A. (2007). Exercise alone reduces insulin resistance in obese children independently of changes in body composition. *Journal of Clinical Endocrinology & Metabolism, 92, 4230-4235.*

Bent, S.C. (1986). Hormonal alterations due to exercise. *Sports Medicine, 3,321-346.*

Bergman, B.C., Horning, M.A., Casazza, G.A., Wolfel, E.E., Butterfield, G.E. & Brooks, G.A. (2000). Endurance training increases gluconeogenesis during rest and exercise in men. *American Journal of Physiology, Endocrinology & Metabolism, 278,1244-1251.*

Berggren, J.R., Hulver, M.W., Dohm G.L., & Houmard, J.A. (2004). Weight loss and exercise: implication for mscle lipid metabolism and insulin action. *Medicine & science in Sport & Exercise.86, 1191-1195.*

Berggren, J.R., Boyle, K.E., Champman, W.H., & Houmard, J.A. (2008). Skeletal muscle lipid oxidation and obesity: influence of weight loss and exercise. *Journal of physiology, Endocrinology & Metabolism, 294, E726-E732.*

Bergstrom, J. & Hultman, E. (1966). Muscle, glycogen synthesis after exercise: an enhancing factor localized to the muscle cells in man. *Nature, 210, 309-310.*

Betaman, L.A., Start C.A.,Willis, L.H., Houmard, J.A. & Kraus, W.E. (2011). Aerobic exercise yields greatest benefit for metabolic syndrome. *American Journal of Cardiology, 1; 888-997.*

Bjornholm, M., Kawann, Y., Lehtihert, M. & Zierath, J.E. (1997). Insulin receptor substrate-1 phosphorylatin and phosphatidylinositol 3-kinase activity in skeletal muscle from NIDDM subjects after in vivo insulin stimulation. *Diabetes, 46, 524-533, 527.*

Blair, S.N., Kohl, H.W., Paffenbarger, R.S., Clark, D.G, Cooper, K.H, & Gibbons, L.W. [1989]. Physical fitness and all-cause mortality: a prospective study of healthy men and women. *JAMA, 262; 2395 – 24 01*

Blessing, D.L., Keith, R.E. & Williford, H.N. (1995). Blood lipids and physiological response to endurance training in adolescents. *Pediatric Exercise Science, 7, 192-202*

Boden , M., Prince, T.B. & Perseghin, G. (1996). Mechanism of free fatty acid-induced insulin resistance in human. *Journal of Clinical Investigation, 97:2859-2865.*

Boden, G., Lebased, B., Schatz, M., Homko, C. & Lomieuri C. (2001). Effects of acute change of plasma free fatty acids on intracellular fats content and insulin resistance in healthy subjects. *Diabetes, 50,1612-1617.*

Bonora, E., Moyhutte, P., Zankanaro, G., Cigolini, M., Querena, M., & Cacciatore, V. (1989). Estimation of in vivo insulin action in man: comparison of insulin tolerancetest with euglycemic and hyperglycemic glucose clamp studies. *Journal of Clinical Endocrinology & Metabolism, 68,374-378.*

Borg, G.A.V. (1998). *Borg's Perceived* Exertion *and Scale*; Champaign, IL: Human Kinetics

Borg, G.V. & Linderholm, H. (1969). Perceived exertion and pulse rate during graded exercise in various age groups. *Acta Medica Scandinavica 472(suppl): 194-206.*

Borghout, L.B. & Keizer, H.A. (2000). Exercise and insulin sensitivity: a review. *International Journal of Sports Medicine 21, 1-12.*

Boule, N.G., Haddad, E., Kenny, G.P., Wells, G.A. & Sigal, R.J. (2001). Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta- analysis of control clinical trials. *JAMA 286, 1218-1227.*

Boule, N.G., Weisnage,l S.J. & Likka, T.A. (2005). Effect of exercise training on glucose honeostasis: the heritage family study. *Diabetes Care, 28; 120-126*

Boushed, R., Gnaiger, E., Schjerling, P., Skovbro, M., Kraunsoe, R. & Dela, F. (2007). Patients with type 2 diabetes have normal mitochondrial function in skeletal muscle. *Diabetologia, 50, 790-796.*

Bowen, R. (1999). Glucagon. *Endocrine Index of Glossary: 1-2.*

Brandy, M.J. & Saltiel, A.R. (2001).The role of Protein phosphate in insulin action. *Recent Program of Home Research, 56,157-173.*

Brooks, B.A., Faley T.D., & Baldwin K.M. (2005). *Exercise Physiology, Human Bioenergetics and its Application (4th Ed).*New York McGraw Hill Pg 59 -63 & 125.

Brouns, F. & Cargill, C. (2002). *Essentials of Sports Nutrition*; England; John Wiley and Sons Ltd., p. 34.

Bunt, J.C., Salbe, A.D., Harpe,r T., Hanson, R.L. & Tataranni, P.A. (2003), Weight, adiposity and physical activity as determinant of an insulin sensitivity index in Pinna Indian Children. *Diabetes care, 26;2524-2530*

Calbat, J.A.L. & Maclean D.A. (2002). Plasma, glucagon (1), and insulin responses depend on the rate of different protein solution on humans. *Journal of Nutrition, 132, 2174-2182.*

Cartee, G.D. & Holloszy J.O. (1990). Exercise increases susceptibility of muscle glucose transport to activation by various stimuli. American *Journal of Physiology, Endocrinology and Metabolism, 258:E390-E393.*

Cartee G.D., Young, D.A., Sleeper, M.D., Zaerath, J., Walberg-Henriksson, H. & Holloszy J.O. (1989). Prolonged exercise in insulin- stimulated glucose transport in muscles after exercise. *American Journal of Physiology, Endocrinology & Metabolism, 256; E494-E499*

Cettour-Rose, B., Samee, S. & Russell, A.P. (2005). Redistribution of glucose from skeletal muscle to adipose tissue during catch-up fat: a link between catch-up growth and later metabolic syndrome. *Diabetes, 54, 751-756.*

Chalkley S.M. Hettiarachchi, M., Chisholm, D.J. & Kragan, E.W. (1998). Five-hour fatty acute elevation, increases muscle lipids and impairs glycogen synthesis in the rat. *Metabolism, 47,1121-1126.*

Chen, YD-L., Coulston, AM., Zhou, M.Y., Hollenbeck, CB. & Reavens, GM. (1995).Why do low-fat high-carbohydrate diets accentuate postprandial lipemia in patients with NIDDM? *Diabetes Care, 18, 10-16.*

Chen, YD-L, Swami, S., Skowronski, R., Coulston, A.M. & Reavens, G.M. (1993). Effect of variations in dietary fat and carbohydrate intake on postprandial lipemia in patients with noninsulin dependent diabetes mellitus. *Journal of Clinical Endocrinology and Metabolism, 76, 347-351.*

Choi, C.S., Lee, F.N., & Youn, J.H. (2001). Free fatty acids induce peripheral insulin resistance without increasing muscle base cosimunine pittiway product levels in rats. Diabetes, 50, 415-524.

Chris, A. (2012).The 20 benefits of aerobic exercise. *www.knowyourlife.com (retrieved 3-12-2012)*

Christ-Roberts, C.Y., Pratipanawatr,T., Barria, R., Delport, Kashyap, S. & Mandarino, J. (2004). Exercise training increases glycogen synthase activity and GLUT-4 expression but not insulin signaling in overweight nondiabetic and type 2 diabetic subjects. *Metabolism, 53, 1233-1242.*

Ciccone, C.D. (2002). *Pharmacology in Rehabilitation*. Pennsylvania; F.A. Davis.

Coggan, A.R. (1991). Plasma glucose metabolism during exercise in humans. *Sports Medicine, 11 (2); 102-124.*

Coggan, A.R., Swanson, S.C., Mendenhall, L.H., Habash, D.L. & Kien, C.L. (1995). Effect of Endurance training on, glycogenolysis and gluconogenesis during prolong exercise in men. *American Journal of Physiology, 268, E179-E183.*

Cohen, P. (1993). Dissection of the protein-phosphorylation cascaders involved in insulin and growth factor action. *Biochemistry & Social Trans, 21, 555-567*

Coker, R.H., Hays, N.P., William, R.H., Pbrown, A.,D., Freeling, S.A., Korterbein, P.M., Sullivan, D.H., Starling R.D. & Evans W.J. (2006). Exercise-induced changes in Insulin action and glycogen metabolism in elderly adults. *Medicine & Science in Sports & Exercise, 433-438.*

Coker, R.H. & Kjaer, M. (2005). Glucose regulation during exercise: the role of the neureoedocrine system. *Sports Medicine, (Aucklang N2) 35, 575-583.*

Colberg, S.R. & Crieco C.R. (2009). Exercise in the treatment and prevention of diabetes. *Current Sport Medicine Report, 8(4); 159-175.*

Consumer Union, (1998). Do you know your triglyceride? *Consumer Reports on Health, 10 (11), 7-8.*

Consumer Union, (2005). Which alternative treatments work? Consumer Reports 70 (8); 39-43

Couillard, C., Depress, Jean- Pierre; K., Kamarche, B., Bergeon, J, Gagnon, J, Leon, AS, Rae D.C, Skinner J.S, Wilmore, JH. & Bouchard, C. [2001] Effect of endurance exercise training on plasma HDL-Cholesterol levels depend on levels of triglycerides: Evidence from men of the Health Risk Factors, Exercise Training and Genetics (HERITAGE) Family Study. *Arteriosclerosis, Thrombosis & Vascular Biology, 21, 1226-1232.*

Craig, W.Y. (1998). Lipoprotein (a) as risk factor for ischemic heart disease: meta-analysis of prospective studies. *Clinical Chemistry, 44, 2301-2306.*

Cruz, M.l., Weigensberg, M.J., Huang, T.F, Ball, G., Shaibi, G.O. & Goran M.I. (2004).The metabolic syndrome in overweight Hispanic youth and the role of insulin sensitivity. *Journal of Clinical Endocrinology & Metabolism, 89, 108-113.*

Cryer, P.E. (2001). *The Endocrine Pancreas and Regulation of Metabolism. In;* Fefferson L.S. & Cherrington, A.S.(Eds). *Handbook of Physiology*; New York; Oxford University Press.

Defronzo, R.A., Tobin, J.D., & Andres, R. (1979). Glucose clamp technique: a method for quantifying insulin secretion and resistance. *American Journal of Physiology, 237, E214- E223.*

DeFronzo R.A., Jucol, E., Jequer, E. Maeder E., Walmren, J. & Felber, J.P. (1981). The effect of insulin on the disposal of intravenous glucose: Results from indirect calomentry and lipitic, and forward venous cathetenization. *Diabetes, 30, 1000-1007.*

Dekker, M.J., Lee, S., Hudson, R., Kilpatrick, K., Graham, T.E., Ross, R. & Robinson, L.E. (2007). An exercise intervention without weight loss decreases circulating interleukin-6- in lean and obese men with and without type 2 diabetes mellitus. *Metabolism, 56, 332-338.*

Deklin, J.T. & Ruderman, N. (2002). *Diabetes and Exercise*: *The Risk*, *Benefits Profile Revisited*. *In*: *Handbook of Exercise in Diabetes*. Ruderman, N. Devlin, J.T., Schneider, S.H. & Krisra, A. (Eds). Alexandria, VA; *American Diabetes Association*.

Dela, F., Larsen, J.J., Mikines, K.J., Ploug, T., Peterson, L.N. & Galbo, H. (1995). Insulin-stimulated glucose clearance in patient with NIDDM. *Diabetes, 44, 1010-1020*

Dela, F., Mikines, K.J., Linstow M.V, Secher NH. & Galbo, H. (1992]. Effect of training on insulin mediated glucose uptake in human skeletal muscle. *America Journal of Physiology, Endocrinology and Metabolism, 263E; 1134-1143*

Department of Human Services, (1996). *Physical Activity and Health: A Report of the Surgeon General. Centers for Disease Control and Prevention, National Center for Chronics Disease Prevention and Health Promotion.* Washington, D.C. U.S Government Printing Office

Depress J.P [1994] Dysliipidemia and Obesity. *Bailers Clinical Endocrinology and Metabolism 8; 629-660*

Devlin, J.F., Hirshman, M.F., Horton, E.S. & Horton, E.D. (1987). Ehanced peripheral insulin and insulin sensitivity in NIDDM after single bout of exercise.*Diabetes 36, 434-439.*

Diabetes Control and Complications Trials Research Group, (1993). The offer of metabolic treatment of diabetes on the development and progression of long term complication in insulin dependent diabetes mellitus. *New England Journal of Medicine, 329, 977-86*

Diabetes Control and Complication Trial Research Group (1996).The absence of a glycermic threshold for the development of long- term complications: The Perspective of the Diabetes Control and Complication Trial. *Diabetes*, *45*(*10*); *1289-1298*

Diabetes Prevention Programme Research Group, (2005). Reductions in the incidence of type 2 diabetes will lifestyle intervention or malformation. *New England Journal of Medicine*, *346*, *393-403*.

Diabetes Prevention Programmed Research Group; Knower, W.C., Barrett-Connore, Fowler, S.E., Hamman, R.F., Lachin, J.M., Walker, E.A. & Nathan, D.M. (2002). Reduction in the incidences of type 2 diabetes with lifestyle intervention on metformin. *New England Journal of Medicine, 346, 393-403.*

Dishman, R.K. (1994). Prescribing exercise intensity for healthy adults using rating perceived exertion. *Medicine and Science in Sport and Exercise 26, 1087-1094.*

Dresner, A., Laurent, D. & Macucci, M. (1999). Effect of free fatty acids on glucose transport and insulin resistance associated phosphatidynositol 3-kinase activity. *Journal of Clinical Investigation, 103: 253-259.*

Drouin, R., Lavoie, C., Bourque, J. Durcos, F., Possion, D. & Chiasson, J.L. (1998). Increased hepatic glucose production, response to glucagon in trained subjects. *The American Journal of Physiology, 274, E23-E28*

Drygas, W., Kostka, T., Jegier, A. & Kunski, H. (2000). Long-term effects of different physical activity levels on coronary disease factor in middle-aged men. *Journal of Sports Medicine, 21, 235-241.*

Dullo, A.G. (2005). A role for suppressed skeletal muscle thermogenesis, in pathways, from weights, flutalon to the insulin resistance. *Alta Physiology of Science, 184, 295-307.*

Dunning B.E., Foley, J.E. & Ahren, B. (2005). Alpha cell function in health and disease; influence of glucagon like peptide -1. *Diabetologia*, 48 (9); 1700-1713

Durstine, J.L., Grouse, S.F. & Moffatt, R. (2001). *Lipids in Exercise and Sports*. In Briskell, W. & Wolinsky, J. (eds.). *Energy*, *Yielding Macronutrients and Energy Metabolism in Sports Nutrition*, Vol. II.; Boston (FL); CRC Press; 87-117.

Durstine, L., Peter, W.G., Paul, G.D., Michael, A.J., Mathew, L.A. & DuBose, K.D. (2002). Blood lipids and lipoprotein adaptation Co-exercise: A qualitative analysis. *Sports AVU Medicine, 13, 50-62.*

Edelmann, E., Staudner, v. & Bachmann, w. (1986). Exercise induced hypoglycemiaand subcutaneous insulin infusion. *Diabetologia, 3, 526-531.*

El-hazmic, LMA. & Warsy, A.S. (1994). Lipid profiles in Saudi non-insulin dependent diabetic patients. *International Diabetes Digest, 5,21-24.*

Ellis, B.A., Poynten, A. & Lowy, A.J. (2000). Long-chain acyl-Co Aesters as indicators of lipids metabolism and insulin sensitivity in rat and human muscles. American *Journal of Physiology, Endocrinology and Metabolism, 279, E554-E560.*

Emoto, M., Klarrhund, J.K., Waters, S.B., Hu, V., Buxton, J.M., Chwla, A. & Czech N.P. (2000). The role of phospholipids signaling system and glucose transport translocation. *Journal of Biochemistry, 275, 7144-7157.*

Endocrine Web, (1998). Normal regulations of blood glucose levels .*Available at www.endocrineweb.com (retrived 16/7/2012).*

Evans, E.M., Van, Pelt, R.E., Binder, E.F., Williams, D.B., Ehsan, A.A. & Kohrt, W.M. (2001). Effects of H.R.T. and exercise training on insulin action, glucose tolerance, antibody composition in older women. *Journal of Applied Physiology, 90, 2033-2040.*

Executive summary of the third report of the national cholesterol education program (NCEP) (2001). Experts panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adults Treatment Panel 111). *JAMA, 285, 2486-2497*

Facchini, F.S., Hu, N., Abbasi, P. & Reavens, G.M. (2001). Insulin resistance as a predictor of age-related diseases. *Journal of Clinical Endocrinology & Metabolism, 86, 3574.-3578.*

Fargular J, W, R., Frank, A, Gross, R..C. & Reavens, G, M. (1996). Glucose, insulin, and triglyceride responses to high and low carbohydrate diet in man. *Journal of clinical Investigation, 45,1645-1656.*

Farhan, M. & Michael, M. (2008). Low high-density lipoprotein cholesterol: an important consideration in coronary heart disease risk assessment. *Current opinion in endocrinology, diabetes and obesity, 15, 175-181.*

Felig, P. and Wahren, J. (1975). Fuel Homeostasis in exercise. *New England Journal of Medicine, 293,10078-1084.*

Fell, R.D., Terblanche, S., Ivy, J.L., Young, J.C. & Holloszy, J.O. (1982). Effects of muscle glycogen content on glucose uptake by muscle following exercise. *Journal of Applied Physiology, 52, 434-437.*

Feranmini, E., Barrett, E.J., Bevilaeyua, S. & De Fronzo, R.A. (1983). Effect of fatty acids on glucose production and utilization in man. *Journal of Clinical Investigation, 72, 1737-1747.*

Ferguson, M.A., Gutin, B., Le, N.A., Karp, W., Litaker, M., Humpries, M., Okuyama, T., Riggs, S. & Owen, S. (1999). Effect of exercise training and its cessation on component of the insulin resistance syndrome in obese children. *International Journal of Obese Related Metabolic Disorders 23; 889-895.*

Fisher, J.J., Gao, J., Han, D.H., Holloszy, J.O., & Nolte, L.A. (2002). Activation of amp kinase enhances sensitivity of muscle glucose transport to insulin. *American Journal of Physiology, Endocrinology & Metabolism, 282, e18-e23.*

Fisher, J.S., Gao, J., Han, H.H., Holloszy, S.O. & Nolte, L.A. (2008). Activation of AMP-Kinase enhanced sensitivity of muscle glucose transport to insulin. *American Journal of Physiology, Endocrinology & Metabolism, 282, E18-E23.*

Ford, E.S. (2005). Risk for all-cause mortality, cardiovascular disease, and diabetes association with the metabolism syndrome.: a summary of the evidence. *Diabetes Care, 28, 1769-1778*

Folsom A.R, Ameti DK, Hutchinson, RG, Liao F, Clegg L & Cooper L.S, [1997]. Physical activity and incidence of coronary heart disease in middle age women and men. *Medicine in Science Sports and Exercise, 29; 901-909.*

Frankel, S., Elwood, P. & Sweetum, P. (1996). Birthweight, adult risk factor and incidence of CHD. *New England Journal of Medicine, 327, 13350-13355*

Galbo, H. *(1983). Hormonal and Metabolic Adaptation to Exercise.* New York*:* Thiemestratetton*.*

Galbo, H., Holst, J.J. & Christensen N.J. (1975). Glucagon and plasma catecholanine, response to graded and prolonged exercise in man. *Journal of Applied Physiology, 38, 70-75.*

Galbo, H., Richler, E.A. Hilsted J. Holst, J.J., Christensen, N.J. & Henricksson, J. (1977). Hormonal regulation during prolonged exercise. *Annals of New York Academy of Science, 301,72-80.*

Galbo, H., Holst, J.J. & Christensen, N.J. (1972). Glucagon plasma and prolonged exercise in Man. *Journal of Applied Physiology, Respiratory, Environmental & Exercise physiology, 38, 70-76.*

Gallian,T. & Burke M.D. (1978). Effect of exercise on serum lipid and lipoprotein in girls, Ages 8 to 10 years. *Artery, 4; 203-213*

Galloway, M.T. & Jokl, P. (2000). Ageing successfully: The importance of physical activity in maintaining health and function. *Journal of American Academy, Orthopedics Surgery, 8, 37-44.*

Ganong, W.F. (2001).*Endocrine Functions of the Pancreas and Regulation of Carbohydrate Metabolism. In Review of Medical Physiology;* New York; McGraw-Hill, 322-343.

Gardner C.D. & Kraener, H.C. (1995). Monounsaturated versus polyunsaturated dietary fat and serum lipids: a meta analysis. *Arteriosclerosis, Thrombosis & Vascular* Biology, *15, 1917-1927.*

Garg, A. Bantte, J.P., Henry, R.R., Coulston A.M., Griver K.A. et al; (1998). Effects of varying carbohydrate content of diet in patients with insulin dependent diabetes mellitus. *JAMA, 271, 1421-1428.*

Golbourt, l., Yaari, S. & Medalic, J.H. (1997). Isolated high density lipoprotein- chplesterol as risk factor for coronary heart disease mortality: 21 year follow up of 8000 men. *Arteriosclerosis*, *Thrombosis & Vascular Biology, 17, 107-113.*

Goodman, E. & Whitaker, R.C. (2002).A prospective study of the role of depression in the development of persistence of adolescent obesity. *Pediatrics 110*(*3*); *497-504*

Goodpaster, B.H., Katsiaras, A. & Kelley, D.E. (2003). Enhanced fat oxidation through physical activity is associated with improvements in insulin sensitivity in obesity. *Diabetes, 52, 2191-2197.*

Goodpaster, B.H., Thaete, F.L., Simoneau, J.A. & Kelley, D.E., (1997). Subcutaneous abdominal fat and thigh muscle composition predict insulin sensitivity independently of visceral fat. *Diabetes, 46 (10); 1579-1585.*

Goodwin, M.L. (2010). Blood Glucose regulation during prolonged, submaximal continuous exercise: A Guide for clinicians. *Journal of Diabetes Science & Technology, Volume 4, Issue 3, 694-705.*

Goodyear, L.J., Giorgeno, F., Sherman, L.A., Carey, J., Smith, R.J., & Dohm, G.L. (1995). Insulin receptor, phosphorylation, and phosphatidylonisitol 3-kinase activity are decreased in intact skeletal muscle strips from obese subjects. *Journal of Clinical Investigation, 95:2195-2201.*

Goodyear L.J, & Smith, R.J., [1994] *Exercise and Diabetes*; *in Joslin's Diabetes Mellitus*; Kahn, C.R. (Eds); Philadelphia; Lea Febiger, Pp 451 – 459

Grassi, J. & Pradelles, P.H. [1991] Compounds Labelled The Acetylcholonesterase Of Electrophone; Its Preparation Process And Its Use As A Tracer Of Marquer In Enzymes-Immunological Determinations. *United State Patent, N I: 047, 330*

Gratton, C. & Jones, I. (2004). *Research methods for sports studies*: New York, Routledge.

Greenspan, F.S. & Gardner, D.G. (2004). *Basic and Clinical Endocrinology*. New York; Mcgraw Hill

Greiwe, S.S., Hickner, R.C., Hansen, P.A., Racette, S.B., Chen, M.M. & Holloszy, J.O. (1999). Effects of Endurance Exercise training on Muscle Glycogen accumulation in humans, *Journal of Applied Physiology, 37, 222-226.*

Griffin M.E., Marculli, N.J. & Cline, G.W., (1999). Free fatty acid-induced insulin resistance is associated with activation of protein kinase-etheta and alteration in the insulin signaling cascade. *Diabetes, 48, 1270=1274.*

Gulve, E.A., Cartee, G.D., Zieratte, J.R., Corpus, V.M. & Holloszy, J.O., (1990). Reversal of enhanced muscle glucose transport after exercise: Roles of insulin and glucose. American *Journal of Physiology, Endocrinology & Metababolism, 259, E685-E691.*

Guo, W., Kawano, H., Piao, L., Itoh, N., Node, K. & Sato, T.(2011). Effects of aerobic exercise on lipid profiles and high molecular weight adiponectin in Japanese workers. *International Medicine, 50 (5), 389-395.*

Gutin, B., Barbeau, P., Owens, S., Lemmon, C.R., Bauman, M., Alisson, J., Kang, H.S. & Litaka, M.S. (2002). Effects of exercise intensity on cardiovascular fitness, total body composition, visceral adiposity of obese adolescents. *American Journal of Clinical Nutrition, 751, 318-326*

Guyton,A. & Hall, J. (2006). *Textbook of Medical Physiology*. Philadelphia; Elsevier Saunders.

Guyton, A. Hall, J. (2011). Textbook of medical physiology (12th edition); Phyladelphia; Elsevier Saunders, pp 809-830.

;

Gyntelberg, F., Rennie, M..J, Hickson, R.C. & Holloszy, J.0.(1977). Effect of training on the responses of plasma glucagon to exercise. *Journal of physiology, 43 (2), 302-305*

Habibzadeh, N. (2010). Effects of aerobic exercise on some selected metabolic syndromes in young obese women. *Acta Kinesiologic, 4, 24-27.*

Haddad, F. & Adams, G.R. (2002). Exercise effects on muscle insulin signaling and action selected contribution: Acute cellular and molecular responses to resistance exercise. *Journal of Applied Physiology, 93, 394-403.*

Hassen, P.A., Nolte, L.A., Chen, M.M., & Holloszy J.O. (1998). Increase GLUT-4 translocation mediates enhanced insulin sensitivity of muscle glucose transport after exercise. *Journal of Applied Physiology, 85, 1218-12221*

Hartley, L.H., Mason, J.w., Hoggan, R.P., Jorus, L.G., Kotchen, T.A., Mougey, E.H., Wherry, F.E., Pennington, L.L., & Ricketts, P.T. (1972). Multiple hormonal responses to prolonged exercise in relations to physical training. *Journal of Applied Physiology, Respiratory, Environment & Exercise Physiology, 53, 607-610.*

Hawley, J.A. & Lassard, S.J. (2008). Exercise training induced improvement, in insulin action. *Acta Physiology (Oxf.), 192(1): 127-135.*

Hegarty, B.D., Cooney, G.S., Kraegan, E.W. & Furler, S.M. (2002). Increased efficiency in fatty acid uptake contributes to liipid accumulation in skeletal muscles of high fat fed insulin resistance rats. *Diabetes, 51, 1477-1484.*

Hegarty, B.D., Furler, S.M., Ye, J., Cooney, G.S. & Kraegen, E.W. (2003).The role of intramuscular lipid in insulin resistance. *Acta Physiology of Scandinavia., 178, 373-383.*

Heled, Y., Shapiro, Y., Shani, Y., Maran, D.S., Langzam, L., Barash, V., Sampson, S.R. & Mayeovital, N.J. (2004). Physical Exercise enhances hepatic insulin signaling and inhibits phosphanol pyruvate carboxylaminase activity in diabetes prone pammony obese. *Metabolism, 53, 836-841.*

Heyward, VH.(1997). *Advanced Fitness Assessment and Exercise Prescription (3rd Ed);* champaign*;* Human Kinetics*.*

Holloszy, J. & Narahara, H.T.C., (1965). Studies of tissue permeability Changes impermeability to 3-methylglucose associated with contraction of isolated frog muscles.*Journal of Biological Chemistry, 240, 3493-3500.*

Holloszy, J.O. (2005). Exercise-induced increase in muscle insulin sensitivity. *Journal of Applied Physiology, 99(1), 338-343.*

Holloszy, J.O. & Hansen, P.A. (1996). *Regulation of Glucose Transport into Skeletal Muscle in: Review of Physiology, Biochemistry, and Pharmacology:* edited by, Blaustein, M.P., Goumidce, H., Habermann, E., Pette, D., Schultz, G. & Schwaieger, M.: Berlin; Springer-Verlag, Pg. 99-193.

Holloszy, JO. (2013). Role of exercise in reducing the risk of diabetes and obesity: Exercise induced increase in muscle insulin sensitivity. *Journal of Applied Physiology, 99, 338-343.*

Hovorka, R., Canonico, V., Chassin, IJ., Haveter, U., Massi-Benedetti, M., Orsin-Federia, M., Pieber, T.R., Schaller, H.C., Schaupp, L., Vering, T. & Wilinska, M.E. (2004).Nonlinear model predictive control of glucose concentration in subjects with type 1 diabetes. *Physiology, 25(4), 905-920.*

Huang, T.T., Ball, G.D. & Frauls, P.W. (2007). Metabolic Syndrome in Youth: Current Issues and Challenges. *Journal of Applied Physiology, Nutrition and Metabolism, 32, 13-22.*

Hu, F.B. (2003). Sedentary lifestyle and risk of obesity and T2D. *Lipids, 38, 103-108*

Hu, F.B. & Manson, J.E. (2003). Walking; the best machine for diabetes. *Arch International Medicine, 168, 1397 -1398*

Hussein, N.Y., Christin, M.A., Raji, K.K., Thomas, R.V., Frank, K. & John, P.K. (2009). Effect of exercise and caloric restriction on insulin resistance and cardiometabolic Risk factor in older obese adults: a randomized clinical trial. *Journal of Gerontology, 64 (1), 90-95*

Imperatore, G., Cheng, Y.J., Williams, D.E., Fulton, J., & Gregg, E.W. (2006). Physical activity, cardiovascular fitness and insulin sensitivity among U.S. adolescents: the national health and nutrition examination survey 1999-2002. *Diabetes care 29, 1567-1572.*

Irwin, M.L., Mayer-Davis, C. & Addy, L. (2000). Moderate Intensity physical activity and fasting insulin levels in women. *Diabetes Care, 23,449-454.*

Itani, S.I., Ruderman, N.B., Schmieder, F. & Boden, G. (2002). Lipid-induced insulin resistance in human muscle is associated with changes in diacyalycerol, Protein universal and IKB-alpha. *Diabetes, 51, 2005-2011.*

Jacobson, T.A., Miller, M. & Schaefer, E.J. (2007). Hypertriglyceridemia and cardiovascular risk reduction. *Clinical Therapeutics, 29, 763-777.*

Jonas, s, 2001. Weighing in on the obesity epidemic: what do we do now? *American College of Sport Medicine's Health & Fitness Journal, 5, (5), 710*

Jansen, I., Fortier, A., Hudson, R. & Ross, R. (2002). Effects of an energy restrictive diet or without exercise on abdominal fat, intramuscular fat, and metabolism risk factors in obese women. *Diabetes Care, 25, 431-438.*

Jatau, R.S., Venkateswarl, K., Dikki, C.E. & Haruna, F.R. (2012). Effects of moderate intensity interval training on running on lipids and lipoproteins of sedentary Nigeria male adults. *Journal of Health, Physical Education, Sports and Leisure Studies. Vol. 3, No. 2, 144-155*

Jentjens, R.L.P..G, Veriables, M.C. & Jeukendrup, A.E. (2004). Oxidation of exogenous glucose, sucrose and maltose during prolonged cycling exercise. *Journal of Applied Physiology 96, 1285-1291*

Kadoma, S., Tanaka, S., salto, K., Shu, M., Sone, Y., Onitake, F., Suzuki, E., Shimano, H., Yamamoto, S., Kondoo, K., Ohashi, Y., Yariada, N. & Sone, H. (2007). Effect Of aerobic exercise training on cholesterol. *Arch International Medicine 167(10), 999-1008*

Kahn, C.R. (1978). Insulin resistance, insulin sensitivity, and insulin unresponsiveness: a necessary distinction. *Metabolism, 27, (supp. 2), 1893-1902.*

Kang, H., Greenson, J.K., Omo, J.T., Chao, C. & Palema, D. (2004). Metabolic syndrome is associated with greater histologic severity, higher carbohydrate, and lower fat diet in patients with NAFLD. *American Journal of Gastro-Enteriology,101, 2247- 2253.*

Kang, H.S., Gutin, B., Barbeau, P., Owens, S., Lemmon, C.R., Allison, J., Litaker, M.S., &Le, N.A. (2002). Physical training improves insulin resistance syndrome in obese adolescents. *Medicine in Sports &Exercise, 34, 1920-1927*

Kang, J., Robertson, R.J., Hagbert J.M. Kelley, D.E., Goss, F.L. Dastiva, S.G., Suminski, R.R. & Utter A.C. (1996). Effect of exercise intensity on glucose and insulin metabolism in obese Individuals and obese NIDDM patients. *Diabetes Care, 19 (4), 311-319.*

Kelley, D.E. Goodpaster, B., Wing, R. R. & Simoneau, J.A. (1999). Skeletal muscle fatty acid metabolism in association with insulin resistance, obesity and weight loss. *American Journal of Physiology, 277, E1130-E1141.*

Kelley, G.S., Kelley, K.S. & Vu Tran, Z.U. (2004). Walking, lipids, and lipoproteins, meta-analysis of randomized controlled trials. *Preventive Medicine, 38, S438-445.*

Kelley, GA., Kelley, K.S. & Vu Tran, Z. [2005].The effect of aerobic exercise on lipid and lipoprotein in overweight and obese adults. International *Journal of Obesity [Lond.], 29 [8], 881-893]*

Kelley, D.E. & Good, P. (2011).Medicine in sports and exercise. *American College of Sport, Medicine, 52, 254-261.*

Kelley, W. (2012). Interval training and diabetes: beneficial or potential harmful.post action to time line. *http//www.flickr.com.photos 1270 650@no51*

Kelley, D.E., Mokan, M., Simonean, J.A. & Manderino, L.J. (1993). Interaction between glucose and free fatty acid metabolism in human skeletal muscle. *Journal of Clinical Investigation, 92, 91-98.*

Kerlinger, fn. (1988). *Foundations of Behavioral Research* (*3rd edition*); New York; Holt Rinehart and Winston; inc.pp299-343.

Khaw, KT., Wareham, N., Bingham, S., Luben, R., Welch, A., & Day, N. (2004). Association of hemoglobin A, C with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. *Annals of International Medicine, 141, 413-420.*

Khoo, E.Y., Wallis, J., Tsentzas, K., Macdonald, I. & Mansell, P. (2010). Effect of exernatide on circulating glucose, Insulin, glucagon, cortisol and catecholamines in healthy volunteers during exercise. *Diabetologia, 53(1), 139-143.*

Khorshidi, D., Assarzadeh, M., Beni, B., K., Abedi, B., & Ezadi, M. (2012). The effect of period of selective aerobic exercise on serum level of leptin and some hormones in obese men. *Annals of Biological Research, 3 (3), 1415-1423.*

Kim, H.S., Abbasi, F., Lamendola, C., MC Laughlin, T. & Reavens, G.M. (2001). Effect of insulin resistance on postprandial elevations of remnant lipoprotein concentration in postmenopausal women. *American Journal of Clinical Nutrition, 74, 592-595.*

Kim J.K., Fulmore, J.J. & Chen, Y. (2000a). Tissue specific overexpression of lipoprotein lipase causes tissue specific insulin resistance. *Proceedings of National Academy of Science, USA. 98, 7522-7572.*

Kim, Y.B., Mikoulina, S.E., Giaraldi, T.P., Hurry, R.R. & Kahn, B.B. (2000b). Normal insulin in A-Zip/F-1 fatter mice. *Journal of Biological Chemistry, 275,456-8460.*

King, D.S., Dalsky, G.P. & Cutter, W.E. (1988). Effect of lack-exercise on insulin secretion and action in trained subjects. *American Journal of Physiology, Endocrinology and Metabolism, 254, E537-E542.*

King H. Albert R, & Herman, W. [1998]. Global border of diabetes. *Diabetes Care, 21, 1414-1431*

King, H. & Kriska, A.M. (1992). Prevention of Type 2 diabetes by physical training: Epidemiological Consideration and Study Methods. *Diabetes Care*, *15*: *1794-1799*

Kjaer, M., Hollenbeck, C., Frey-Hewith, B., Galbo, H., Haskell, W. & Reavens, G. (1990). Glucoregulation and hormonal response to maximal exercise in non- insulin dependent diabetes. *Journal of Applied Physiology, 68, 2067-2074.*

Klein, S., Luu, K., Gasic, & Green, A. (1996). Effect of weight loss on whole body and cellular lipid metabolism in severely obese humans. American *Journal of Physiology, Endocrinology & Metabolism, 270, e39-e745*

Koivisto, V., Soman, V., Nadel, E., Tamborlane, W.K. & Felig, P. (1980). Exercise and insulin: Insulin binding, insulin mobilization and counter regulatory hormone secretion. *Federal Proceedings, 39, 1481-1486.*

Koo, B.K., Han K.A., Ahn. H.J., Jing J.Y., Kim, H.C. & Min, K.W. (2010). The effect of total energy expenditure from all levels of physical activity Vs. Physical activity energy expenditure from moderate to vigorous activity on visceral fat and insulin sensitivity in obese type 2 diabetic women. *Diabetic Medicine DO1 10 1111, 1964-15491.*

Kristiansen, S., Nielsen, J.N., Bourgoin, S., Klip, A., Franco, M. & Richter, E.A. (2001). GLUT-4 translocation in skeletal muscle Studies with a Cell-free Assay; Involvement of phospholipase D. *American Journal of Physiology, Endocrinology & Metabolism, 281, E608-E618.*

Krishna, M.G., Coker, R.H., Lacy, D.B., Zinker, B.A., Halsetti, A.E., & Wasserman, D.H. (2013).Glucagon response to exercise is critical for accelerated lipatic glutamine metabolism and nitrogen disposal. *American Journal of Physiology, Endocrinology & Metabolism 279, E638-E645).*

Laaksonen, D.E. & Sen C.K. [2000]. *Exercise and Oxidation Stress in Diabetes Mellitus. In Handbook of Oxidant and Antioxidant In Exercise;* Sen C.k. (Ed); Amsterdam, Elsevier 1105 – 1136.

Lakka, T.A. & Laaksonen, D.E. (2007). Physical activity in prevention and treatment of the metabolic syndrome. *Applied Physiology in Nutrition and Metabolism 32 (1), 76-88.*

LaMonte, M.J., Blair, S.N., & Church, T.S. (2005). Physical activity and diabetes prevention. *Journal of Applied Physiology 99, 1205-1213.*

Lamarche, B., Despres, J.P., Pouliot, M.C., Prud'homme, D., Moorjani, S., Lupine, P.J., Nadeau,A.,Tremblay, A. & Bouchard,C. (1993). Metabolic hetorogeneity associated with high plama triglycerideor low Hdl- cholesterol levels in men. *Arteriosclerosis Thrombosis, 13, 33-40.*

Landry, G. (2002). "Eight Hormones and Exercise". Hormones and Exercise. *Free News Letter.(Retrived 5/7/2012.)*

Landt, K.W., Campaigne, B.N., James, F.W. & Sparling, M.A. (1985). Effects of Exercise training on insulin sensitivity in adolescents with type I diabetes. *Diabetes Care, Vol. 8, No.5.*

Lavie, C.J., Mailander, L. & Milani, R.V. (1992). Marked benefits with sustained-release niacin therapy in patients with isolated very low levels of high density lipoprotein cholesterol and coronary artery disease. *American Journal of Cardiology, 69, 1083-1085.*

Lavoie, C.J. (2005). Glucagon receptors: effect of exercise and fasting. *Canadian Journal of Applied Physiology, 30 (3), 313-327.*

Lawrence S. Holman, G.D & Zierath J.R. [1997] Effect of insulin on GLUT-4 cell surface content and turn over rate in human skeletal muscles as measure by: The Exofacial Bis- Manic Photolabelling Technichque. *Diabetes, 46, 1965-1969*

Laycock, J.J., & Wise P.H. (1983). *Essential Endocrinology*. New York; Oxford University Press.

Legare, A., Drouin, R., Milot, M., Massiocotte, D.I, Peronnet, F., Massiocotte, G. & Lavoie, C. (2001). Increased density of glucagon receptors in liver from endurance trained rats. *American Journal of Physiology, Endocrinology & Metabolism, 28(1), E193-E196.*

Lee, A.D., Hansen, P.A. & Holloszy, J.O. (1995). Wortmanniun inhibits insulin stimulated but not contraction stimulated glucose transport activity in skeletal muscle. *FEBS Letters, 361, 51-54.*

Lee, M., Kim, J.Q., Kim, J., Ob, H. Park, M. (2001).studies on the plasma lipid profiles and LCAT and CETP activities according to hyperlipoproteinemia phenotype (HLP). *Atheriosclerosis,159,381-389.*

Leon, A.S. & Sanchez, O.A. (2001). Response of blood lipids to exercise training alone or combined with dietary intervention. *Medicine & Science in Sports & Exercise 33,(6 suppl), S502-S515.*

Lesnick, D. (2002). Types of exercise and their effects on blood glucose. *Palo Alto Medical Foundation.*

Libman, J & Arslanian, S.A. (1999). Type 2 diabetes : no longer just an adult disease. *Pediatric Annals 28,589-593.*

Ligtenberg, P.C., Hoekstra, J.B., Bol, E., Zonderland, M.L. & Erkelens, D.W. (1997). Effect of physical training on metabolic control in elderly type 2 diabetic patients. *Clinical Science (Lond), 93127-93135.*

Linder, C.W., Durant, R.H. & Mahauney, O.M. [1983]. The effect of physical conditioning on serum lipid and lipoprotein in white male adolescents. *Medicine & Science in Sport & Exercise 15, 233 – 236*

Lofgren, P., Holfstedt, J., Ryden, M., Thorne, A., Holm, C., Wahrenberg, H. & Arner, P. (2002). Major gender differences in the lipolytic capacity of abdominal subcutaneous fat-cells in obesity observed before long –term weight reduction. *Journal of Clinical Endocrinology & Metabolism 87,764-771.*

Lund, S., Holman, G.D., Schmitz, O. & Peterson, O. (1995). Contraction Stimulates translocation of glucose transporter from that of insulin. *Proceedings of National Academy of Science, USA ,92, 5817-5821*

Magashi, A. (2014). I need information on obesity and overweight: Health Interactive, *Daily Trust News Paper. Nigeria healthinteractive@ hotmail.com.dailytrust sept. 16th, 2014pg 38.*

Makinde, O.A. (2002). Prevalence of overweight and obesity among secondary school students of different socio-economic status in Kano state, Nigeria. *Journal of Health Education, Vol. 16 No 1, 168-178.*

Manninen, A.H. (2004). Protein hydrolysates in sports and exercise: A brief review. *Journal of Sports Science & Medicine 3, 60-63.*

,

Manson, J.E. & Spelsberg, A. [1994] Primary prevention of non-insulin dependent diabetes mellitus. *American Journal of Preventive Medicine 10, 172-184*

Manson, J.E., Nathan, D.M., Krolewski, A.S., Stenpter, M.J., Willet, W.C. & Hennekens, C.H. (1992). A prospective study of exercise and incidence of diabetes among US male physicians. *JAMA, 268,63-67.*

Marlis, E.B., & Vrani, M. (2002). Intense exercise has unique effects on both insulin release and its roles in glucoregulation: Implications for diabetes. *Diabetes Vol. 51, (supplement I), 5271-5283.*

Masaiger, A.o.,Al-Ansari & Al-Mannai, M (2000). Anthrometric of adolescent girls in bahrain, including body fat distribution. *Annals of Human Physiology, 72, 50515*

Mayfield, J. (1998). Diagnosis and classification of diabetes mellitus. *American Family Physician, 1103-1113.*

McArdel, W.D., Katch, F.I. & Katch, V.L., (2010). *Exercise Physiology*: *Nutrition*, *Energy and Human Performance* (*7th ed*). Baltimore; Lippincott Williams & Wilkins.

MCAulay, K.A., Williams, S.M., Mana, J.I. Goulding, A. Chisholm, A. Wilson, N., Story, G., Mclay, R.T., Harpe,r M.z. & Jones, I.E.(2003).Intensive life styles changes are necessary to improve insulin sensitivity: a randomized control trial. *Diabetes Care, 25, 445-452*

McGill, H.C & McMahan, G.A. (2010). Starting early to control all risk factors in order to prevent coronary heart disease. *Clinical Lipidology, 5, 87-93.*

McLaughlin T. Abbasi, F, Cheal, K, Chu, J, Lamendola C, & Reavens, G.M. (2003). Use of metabolic marker to identify overweight individuals who are insulin resistant. *Annals of International Medicine, 139, 802-809.*

Medline Plus, (2012). Metabolic disorders; US National Library of Medicine; *retrieved from http://www nim nih.gov/medline plus/metabolicdiorders. Html)*

Mikines, K.J., Sonne, B., Trorier, B. & Galbo, H. (1989). Effect of acute exercise and detraining on insulin action in trained men. *Journal of Applied Physiology, 66, 704-711.*

Mitrakou, A., Ryan, C., Veneman, T., Mokan, M., Jensen, T., Kiss, I., Durrant, J., Cryer, P.E. & Gerich, J. (1991). Hierarchy of glycemic threshold for couterregulatory hormone secretion, symptoms and cerebral dysfunction. *American Journal of Physiology, 260 (1pt 1): E67-E74.*

Morgan, J., Carey, C., Lincoff, A. & Capuzzi, D. (2004). High density lipoprotein subfraction and risk of coronary artery disease. *Current Atherosclerosis, 6, 359-365.*

Morley, J.E. (1999). An overview of diabetes mellitus in older persons. *Clinical General Medicine, 15, 211-224.*

Muhammad, M.S. (2003). Effects of aerobic exercise training on selected physiological variables in non-insulin dependent diabetics. *Unpublished PhD. Dissertation, Ahmadu Bello University, Zaria.*

Muller, D.C., Elahi, C.D., Tobin, J.D. & Andros, R. (1996). The effect of age on insulin resistance and secretion. A review. *Sanin Nephiol, 16, 289-998.*

f

Narayani, U. & Sudhan R.R. (2010). Effect of aerobic training on percentages of body total cholesterol and HDL-C among obese women. World *Journal of Sport Sciences, 3(1), 33-36.*

Nassis, G.P., Papapntakou, K., Skenden, K., Triandafillopoulou, M., Kavouras, S.A., Yanakaoulia, M., Chrousos, G.P. & Siclosis, L.S. (2005). Aerobic exercise training improves insulin sensitivity without changes in body weight, body fat, adiponectin and inflammatory markers in overweight and obese girls. *Metabolism, 54,14 72-1479.*

Neel, J.V., Weder, A.B. & Julius, S. (1998). Type II diabetes, essential hypertension and obesity as syndromes of impaired genetic homeostasis: the highly genotype hypothesis enters the 21st century. *Prospect Biology & Medicine, 42, 44-75.*

Nishida, Y., Matsubara, T., Tobina, T., Shindo, M., Tokuyama, K. & Tanaka, H. (2010). Effect of low-intensity aerobic exercise on insulin-like growth factor-1 and insulin-like growth factor-binding proteins in healthy men. *International Journal of Endocrinology, Volume 2010, Article Id 452820,1-8.*

Normal regulation of blood glucose levels, (1998). *Endocrine web. Endocrineweb, com, (accessed July, 2012).*

Oakes, N.D., Kennedy, C.J., Jenkins, A.B., Laybutt, D.R., Chisholm, D.J. & Kraegan, E.W. (1994). A new antidiabetes agent- BRL 49693, reduces lipid availability and improves insulin action and glucoregulation in the rat. *Diabetes, 43, 1204-1210.*

Ochei, J. & Okolhalkar, R. (2007). *Medical Laboratory Science: Theory and Practice;* New Delhi; Tata McGraw Hill Pub Comp. Ltd

Oladele, P.O. (2007). *Introduction to Research Methodology*; Lagos; Niyak Print & Publications.

Olefsky, J.M., Farquhar, J,W & Reavens G.M. (1974). Reappraisal of the role of insulin in hypertriglyceridemia. *American Journal of Medicine, 57, 551-560*

Olefsky, J.M, Reavens, G.M. & Farquhar J.W, (1994) Effects of weight reduction on obesity: studies of carbohydrate and lipid metabolism. *Journal of Clinical Investigation, 53, 64-76.*

Ostrow, A.C. & Dwezltoski, A. (1986). Older adults' perception of physical activity participation based on age-role and sex-role appropriateness. *Research Quarterly, Exercise and Sports, 57,167-169.*

Pan, D.a., Lillioja, S., Kriketos, A.N., Milner, M.R., Baur, L.A., Bogardus, C., Jenkins, A.B. & Storhen, L.H. (1997). Skeletal muscle triglyceride levels are inversely related to insulin resistance action. *Diabetes, 46,983-988.*

Pan, V.R., Li, G.W., Hu, Y.H., Wang, W.Y., An, Z.X., Hu, Z.X., Lim, J., Xigo, J.Z., Cao, H.B., Liu, P.A., Jiang, X.G., Jiang, Y.Y., Wang, J.P., Hheng, H., Zhang, H., Bennett, P.H. & Howard, B.V. (1997). Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance :The da qing igt and diabetes study. *Diabetes Care; 20,537-544*

Paollisso, G. & Howard, B.U. (1998). Role of non-esterified fatty acids in the pathogenesis of type 2 diabetes mellitus. *Diabetes Medicine, 15, 360366.*

Parker, R.S., Doyle, F.J. & Peppas, N.A. (1999). A Model-based algorithm for blood glucose control in type 1 diabetic patients.*IEE Trans Biomedical England, 46 (2), 148-157.*

Paterson, JR., Pattigrew, AR., Dominizak, HM. & Small, M. (1991). Sceening for hyperlipidemia in diabetes mellitus. relationship to diabetic control. *Annals of Clinical Biochemistry, 28, 354-358-*

Peirce, N.S. (1999). Diabetes and exercise. *British Journal of Sport Medicine, 33, 161-173.*

Philips, D.L., Caddy, S. & Ilic, V. (1996). Intramuscular triglyceride and muscle insulin resistance in spontaneously hypertensive rats. *Nature and Genetics 27, 156-158.*

Plough, T., Galbo, H., Vinten, J., Jorgensen, M. & Richter E.A. (1987). Kinetics of glucose-transport in rat muscle: effects of insulin and contraction. *American Journal of Physiology, Endocrinology & Metabolism 253, E12-E20.*

Plowman, S.A. & Smith, D.L. (2008). *Exercise Physiology for Health, Fitness and Performance;*Lippincott; Williams and Wilkin

Pollock, M.L. & Wilmore, J.H. (1990). *Exercise in Health and Disease*: *Evaluation and Prescription for Prevention and Rehabilitation* (*2nd ed*); Philadelphia; Saunders

Prioirier, P., Tramblay, A., Broderick, A., Catellier, C., Tancred, G. & Nadeau, A. (2002). Impact of moderate aerobic exercise training on insulin sensitivity in type 2 diabetic men treated with oral hypoglycemic agents: is insulin sensitivity enhanced only in non obese subjects? *Medicine &. Science, 8 (2,) 59-65*

Powers, S.K. & Howley, E. T. (2012). *Exercise Physiology*: *Theory and Application to Fitness and Performance*, (*4th Ed*)., Boston ; McGraw Hill Higher Education.

Prevance, M., Landa, V. & Zideck, V. (2002). Trasgenic rescue of defective CD 36 ameliorates insulin resistance in spontaneous hypertensive rats. *Nature Genetics, 27, 156-158.*

Pruett, E.D. (1970). Glucose and insulin during prolong work stress in men living on different diets. *Journal of Applied Physiology, 28,199-205.*

Randle, P.J., Garland, P.B., Hales, C.N., & Newsholm, E.A. (1963). The Glucose fatty acid cycle. Its role in insulin sensitivity and the metabolic disturbance of diabetes mellitus. *Lancet, 1,785-789.*

Reavens, G.M., Lerner, R.., Stern, M. & Fargular J.W. (1967). Role of insulin in endogenous hypertriglyceridemia. *Journal of Clinical Investigation, 46, 1756-1767.*

Reavens, G.M. (1995).Pathophysiology of insulin resistance in human diseases. *Physiological Revolution, 75, 476-486.*

Reavens, G.M. (1988). Banting Lecture 1995. Role of insulin resistance in human disease.*Diabetes, 37, 1595-1607.*

Reavens, G.M.(2003). Insulin resistance syndrome: definition and dietary approaches to treatment *.Annual Review on Nutrition, doi10.1146/annurew. Nutrition, 24,(01), 2133- 2155.*

Reavens, G. M. (2005). The insulin resistance syndrome: definition and dietary approaches to treatment. *Annual Review on Nutrition, 25, 391-406.*

Reaven, G. M. (1996). Hypertriglyceridemia: the central features of syndrome x. *Cardiovascular Risk Factors*, 6, 29-35.

Reckon Diagnostics P. *Ltd*.[2003]. *Glucose*; an Iso and GMP Certified Company

Reece, J. & Campbell, N. (2002). *Biology* [6^{th} *edition*]; St Francisca CA; Benjamin Cummings.

Richter, E.A., Garatto, L.P., Goodman, M.N., & Ruderman, N.B. (1982). Muscle glucose metabolism following exercise in the rat Increased sensitivity to insulin. *Journal of Clinical Investigation, 69, 785-793*.

Ritchter, E.A., Mikines, K.J., Galbo, H. & Kliens, B.(1989). Effects of exercise on insulin action in human skeleton muscles. *Journal of Applied Physiology, 66, 876-885.*

Rochalu B, Bernt E, Gruber, W. [1974] Enzymatic Besttimmung Des Gesant – Cholesterins in Serum, *Z. Kiln Biochemistry 12: 226.*

Roch-Norlund, A.E., Bergstrom, J. & Altman.G.(1972). Muscle glycogen and glycogen synthetase, in normal objects and in patients with diabetes mellitus. S. Cardiovascular. *Journal of Clinical Laboratory Investigation, 30, 77-84.*

Roden, L. (2000). Perspective, hexosamine and nutrient sensing. *Endocrinology, 141,1922- 1925.*

Rogers, M.A., Yamamoto, C., King, D.A., Hagberg, J.M., Ehsani, A.A. & Holloszy J.O. (1988). Improvement in glucose tolerance after 1 week of exercise in patients with mild NIDDM. *Diabetes Care, 11(8), 613-618.*

Romijn, J.A., Coyle,E.F., Sidoscis, L.S., Gasteldelli, A., Horowitz, J.F., Endert, E. & Wolfe, R.R. (1993). Regulation of androgenous fat and carbohydrate metabolism in relation to exercise intensity and duration. American *Journal of Physiology, Exercise, Endocrinology & Metabolism, 265 (3), 380-391.*

Rorsman, P. (2005). Insulin and glucagon. *British Journal of Diabetes Care and Disease, 5,(45), 187-191.*

Ross, K., Dagnone, D., Jones, P.T., Smith, H. Paddass, A., Hudson, R., & Janssen, I. (2000). Reduction in obesity and related commordbid conditions after diet-induced weight loss or exercise-induced weights loss in men. A Randomized controlled trial. *Annals of International Medicine, 33,92-103.*

Ross, W.B. & Mayfell-Jones, M.J. (1982). Kinanthropometry, Macougal JD Wanger, HA, & Green (Editors). *Physiological Testing of Elite Athletes*; Champaign II; Human Kinetics..

Rossetti, L. (2000). Perspective:Lexosamine and nutrient sensing. *Endocrinology*; *141*:*1922-1925*

Rowe, D.A. (2007). *Measurement for Evaluation in Physical Education and Exercise Science;* Boston; McGraw-Hill Higher Education Company Inc.

Roy, A. & Parker, R. (2007). Dynamic modeling of exercise effect on plasma glucose and insulin levels. *Journal of Diabetes Science and Technology, Volume 1, Issue 3, 338-347.*

Ruderman, N.B., Devlin, J.T., Schineider, S. & Kriska, A. (2001) (editors). *Handbook of Exercise in Diabetes*; Alexandria, VA; America Diabetes Association; chapts 3 & 8-12.

Sarwar, N., Danesh, J., Eiriksdottir, G., Sigurdsson, G., Warehan, N., Bingham, S., Matthijis Boekholdt, S. Khaw, KT., & Gudnason,V. (2007). Triglyceride and the risk of coronary heart disease: 10158

incident cases among 262525 participants in 29 Western prosoective studies. *Circulation, 45, 450-458.*

Sato, Y. (2003). Physical exercise for diabetes mellitus: the effective program for treatment. *Japanese Medical Association Journal: 46, 1-5.*

Sato, Y. (2000). Diabetes and lifestyle: role of physical exercise for primary prevention. *British Journal of Nutrition, 84, 5187-5190.*

Sato, Y., Nagasaki, M., Nakai, N. & Fushimi, T. (2003) Physical exercise improves glucose metabolism in lifestyle related diseases. *Experimental Biology and Medicine, 228, 1208-1212*

Schenk, S. & Horowitz, J.F. (2007). Acute exercise increases triglycerides synthesis in skeletal muscles and prevents fatty acid-induced insulin resistance. *Journal of Clinical Investigation, 117, 1679-1689.*

Schenk, S., Harber, M.P., Shrivastava, C.R., Burrant, C.K. & Horowitz, J.F. (2009). Improved insulin sensitivity after weight loss and exercise training is mediated by reduction in plasma fatty acid mobilization not enhanced oxidation capacity. *Journal of Physiology, 587(28), 4949-4961.*

Schmitz-Peiffer, C., Browne, C.L., & Oakes, N.D. (1997). Alterations in the expression and cellular localization of protein-kinase C. isozymes epsitan and that are associated. *American Journal of Clinical Nutrition, 73, 885-891.*

Sembulingan, K. & Sembulingan, P. (2010). *Essentials of Medical Physiology* (*7th Ed*). St Louis (USA); Jaypee Brothers Medical Publishers (P) Ltd

Shaibi, G.Q., Cruz, M.L., Ball, G.D., Weigensberg, M.J., Salem, G.J., Crespo, N.C. & Goran, M.I. (2006). Effects of resistance training on insulin sensitivity in overweight Latino adolescent males. *Medicine and Science in Sports and Exercise, 38, 1205-1015.*

Shaibi, G.O., Robert, C.K., & Goran, M.I. (2008) Exercise and insulin resistance in youth. *American College of Sport Science, volume 36, No1:5-11*

Sigal, R., Kenny, G.P., Wasserman, D.H., Castandeda-Scoppa, C. & White, R.D. (2006). Physical activity/exercise and type two diabetes: a consensus statement from the American Diabetes Association. *Diabetes Care, 29(6), 1433-1438.*

Sigma- Aldrich. (2013). *Product Information-Glucagon Kit for Serum, Plasma, Culture Supernatant, and Cell Lysates;* USA, e-mail: techservice @ sial.com sigma-aldrich.com

Simmoneau, J.A., Colberg, S.R., Thaete, F.L. & Kelley, D.E. (1995). Skeletal Muscle glycolytic and oxidative enzymes capacities are determinants of insulin sensitivity and muscle composition in obese women. *FASEB 59 (2), 273-278.*

Simpson, E., Whitehead, J.P. & James, D.E. (2001). GLUT 4, at the Crossroad, between membrane trafficking and signal transduction. *Traffic, 2, 2-11.*

Skyler, J.S. (1998). Prevention and treatment of diabetes and its complications. *Med*. *Chin*. *North Am*, *82*, *665*.

Slentz, C.A., Tenner, C.J., Bateman, L.A., Durheim, M.T., Huffman, K.M., Houmand, J.A. & Kraus, W.E. (2009). Effect of exercise training intensity on pancreatic beta cell function.*Diabetes Care, 32(10), 1807-1811.*

Somwar, R., Perreault, M., Kapur,S., Taha, C., Sweeney, G., Ramlal, T., Kim, D.Y., Keen, J., Gote, C.H., Klip, A. & Marette, A. (2000). Activation of P38 nitrogen-activated protein kinase a and β by insulin and contraction in rat skeletal muscle: Potential role in the stimulation of glucose transport. *Diabetes,49, 17994-1800.*

SPI-Bio [2003] *The Rate Insulin Enzyme Immunoassay*; Us Patent N. 5047.330#

Strand, R.D. & Wallace, D.K. (2005). *Healthy for Life: Developing Healthy Lifestyles that Have Side Effect at Permanent Fat Loss;* USA*;* Real Life Press.

Sweeney, G., Somwar, R., Pamlal, I., Volchuk, A. Leyama, A. & Klip, A. (1999). An incubator of P38 mitogen-activated protein-kinase prevents insulin stimulated glucose transporter but not glucose transporter translocation in 3T3-LJ adipocytes and 6 myotubes. *Journal of Biological chemistry, 274,10071-10078.*

Tansey, M.J., Tsalikian, T., Beck, R.W., Marcus, N., Buckinham, B.A., Weinzimer, S.A, Janz, K.E., Kollman, C., Xing, D., Ruedy, K.J., Steffes, M.W., Borland, T.M., Singh, R.J., Tauborlane, W.V. & Diabetes Research Children Network, (Directnet) Study Group, (2006). The effects of aerobic exercise on glucose and counterregulatory hormone concentration in children with type 1 diabetes. *Diabetes Care, 29(1), 20-26.*

Taunton, J.E. & McCargarl, E.L. (1995). Staying alive with diabetes. *Physician Sports Medicine, 23 (3), 53-60.*

Thomas, J.R.; Nelson, J.K. & Silverman, S.J. (2005). *Research methods in* ho *physical activity*. Champaign, Illinois: Human Kinetics.

Thomas, T., Adeniran, S. & Etheridge, G. (2004). Effects of Omega-3 fatty acids supplementation and exercise on low density lipoprotein and high density lipoprotein subtraction. *Metabolism, 53,749-754.*

Thompson, P. Cullinane, E. & Sady, S. (2001). The acute versus the chronic response to exercise. *Medicine and Science in Sports and Exercise, 33(6), S438-S445*

Toledo, F.G.S., Menshikova, E.V., Azuma, K., Railikova, Z., Kelley, C.A., Ritov, V.B. & Kelley, D.E. (2008). Mitochondrial capacity in skeletal muscle is not stimulanted by weight loss, despite increases in insulin action and decrease in intramyocellular lipid contents. *Diabetes, 57, 987-994.*

Toledo, F.G.S., Menshikova, E.V., Rilov, V.B., Azuma, K., Badikova, Z., Delany, J. & Kelley, D.E. (2007). Effect of physical activity and weight loss on skeletal muscle mitochondrial and relationship with glucose control in type 2 diabetes. *Diabetes, 56, 2142-2147.*

Tolfrey, K., Jones A.M. & Campbell, I.G. (2000). The effect of aerobic exercise training in the lipid-lipoprotein profile of children and adolescents. *Sports Medicine, 29 (2), 99-112.*

Torjensen, P.A., Burkeland, K.I., Anderson, S.A., Hjermann, I., Holme, I. & Urdal, P. (1997). Lifestyle changes may reverse development of the insulin resistance syndrome. The diet and exercise study: a randomized trial. *Diabetes care, 20, 26-31*

Treuth, M.J., Hunter, G.R., Figueron-Colon, R. & Goran, M.I. (1998). Effects of strength training on intra-abdominal adipose tissue in obese prepubertal girls. *Medicine and Science in Sports and Exercise 30, 1738-1745.*

Tuomilehto, J., Lindstrom, J., Erickson, J.G., Valle, T.T., Hamaleinen, H., Hanne-Parikka, P., Keinanen-Kukaanemi, S., Laakson, M, Louheranta, A., Rastas, M., Salminen, V. & Uusitupa, M. (2001).Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. *New England Journal of Medicine 344, 1343-1350.*

Tuttle, K.R.., Marker, J.C., Dalsky, G.P., Schwartz, N.S., Shab, S.D., Clutter, W.E., Holloszy, J.O. & Cryer, P.E. (1988). Glucagon, not insulin, may play secondary role in defense against hypoglycemia during exercise. *American Journal of Physiology,254 (6 pt 1), E713-E719.*

Van der Heijden G.S., Toffolo, G., Manesso, L., Saur, P.S.S. & Surehag, A.L. (2009). Aerobic exercise increases peripheral and insulin sensitivity in sedentary adolescents. *Journal of Clinical, Endocrinology & Metabolism, 94 (11), 4292-4299.*

Vantone, C. (2002). Unesterified plant steroids and stanol lower LDL-Cholesterol concentrations, equivalent in hypercholesterolemic persons. *American Journal of Clinical Nutrition, 76, 1272-1276.*

Venkateswarlu, K. (2010). *Exercise for Disease Prevention and Health Promotion;* Zaria; Ahmadu Bello University Press, Ltd., Zaria, Kaduna State, Nigeria.

Venkateswarlu, K. (1982). *Theory of Athlete Training (2nd ed.).* Mimeographed Textbook PHE. Department, Ahmadu Bello University, Zaria, Nigeria.

Voet, D. & Voet, J.G. (1995). *Biochemistry*; New York; John Wiley and Sons.

Wahren, J., Felig, P., Ahlbourg, G. & Jorfeldt, L. (1971).Glucagon metabolism during leg exercise in man. *Journal of Clinical Investigation, 50, 2715-2725.*

Wallberg-Henriksson, H. & Holloszy, J.O. (1985). Activation of glucose transport in diabetic muscles: responses to contraction and insulin. *Cell Physiology, 249, C233-C237.*

Wasserman DH, Gree RJ. Williams PE, Lacy DB & Abeemrad NN (1991) Interaction of GUT and liver nitrogen metabolism during exercise. *Metabolism, 40, 307-314*

Waugh, A. & Grant. A. (2006). *Rose and Wilson Anatomy and Physiology in Health and Illness;* New York; Church Hill Livingstone; p. 222-223

Wayo, I., Gwani, J.A., Chado, M.A. & Haruna F.R. (2012). The roles of aerobic and resistance training programmes in the management of selected risk factors of metabolic syndrome-among adults in Yola. *Nigeria. Journal of Health, Physical Education, Sports and Leisure Studies, vol. 3, no.2: 156-172.*

White C.M [1999]. A review of potential cardiovascular uses of intravenous glucagon administration.*Journal of Clinical Pharmacology, 39, [5], 442-447*

Wildman, R.E.C. and Miller, B.S. [2004]. *Sport and Fitness Nutrition; Australia;* Thomson Wadsworth.

William, M.H. (2007). *Nutrition for Health Fitness and Sport*; Boston; McGraw-Hill, Higher Education.

Wilmore, J.H. & Costill, D.L. (2004). *Physiology of Sport and Exercise*; United State of America; Human Kinetics

World Health Organization, (1998). *Obesity*; *Preventing and Managing the global epidemic*, *Report of WHO Consultant on Obesity*, Geneva; Switzerland, WHO

World Health Organization, (1999).*Definition, Diagnosis and Classification of Diabetes Mellitus And its Complications: Report of WHO Consultation*. Geneva; World Health Organization,(WHO)

Wojtaszewski, J.F.P., Nielsen, J.N., & Richter, E.A. (2002).Exercise effects on muscle insulin signaling and action. Invited review: Effect of acute exercise on insulin signaling and action in humans. *Journal of Applied Physiology, 93, 384-392.*

Wojtaszewski, J.P. Hassan, B.F., Kliens, B. & Richter, E.A. (1997). Insulin signaling in human skeletal muscle time course and offered of exercise. *Diabetes 43, 1775-1781.*

Wojtaszewski, J.F.P., Hassen, B.F.; Gade, J., Kiens, B., Markuns, J.F, Goodyear, LJ. & Richter, E.A. (2000). Insulin signaling and insulin sensitivity after exercise in human skeleton muscles. *Diabetes, 49, 320-325*

Wojtaszewski, J.F., Hiyaki, Y., Hirshman, M.F., Michael, M.D., Dutresne, S.D., Kahn, C.R. & Goodyear, L.T.(1999). Exercise modulates post receptor insulin signaling and glucose transport in muscle-specific insulin receptor knockout mice. *Journal of Clinical Investigation, 104, 1257-1264.*

Wolfe, R.R., Nedel, E.R., Shaw, J.H.F., Stephenson, L.A., & Wolfe, W.H. (1986). Role of changes in insulin and glucagon in glucose homeostasis. *Journal of Clinical Investigations Volumetric, 900-907.*

Wright, D.C., Geiger, P.C., Holloszy J.O. & Han, D.H. (2005). Contraction and hypoxia stimulated glucose transport is mediated by a Ca^{2+} dependent mechanism in slow twitch rate soleus muscle. American *Journal of Physiology, Endocrinology and Metabolism, 288, E1062-E1066.*

Wright, D.C. Hucker, K.A., Holloszy, J.O.& Han, D.H. (2004). Ca^{2+} and AMPK, both mediate stimulation of glucose transport by muscle contraction. *Diabetes, S3, 330-335.*

Yamanouchi, K, Shinozaki, T, Chikada, K, Nishkawa, T., Ito, K., Shinizu, S., Ozawa, N., Suzuki, Y., Maeno, H., Kato, K., Oshida, Y. & Sato, Y. (1995). Daily walking combined with diet therapy is a useful means for obese NIDDM patients not only to reduce body weight but also to improve insulin sensitivity. *Diabetes Care, 18, 775-778*

Ye, J.I., Gulve, E.A., Rameh, I. & Birnbaum, M.J. (1995). The effect of wortmannin in rat skeletal muscle: dissociation of signaling pathway for insulin and contraction-activated hexostransport. *Journal of biological chemistry, 270, 2107-2111.*

Young, J.C., Garthwaite, S.M., Bayan, J.E., Cartier, L.J., & Holloszy, J.O. (1983). Carbohydrate feeding speeds reversal of enhanced glucose uptake in muscle after exercise.. *American Journal of Physiology, 245, R684-R688.*

Young, D.A., Wallberg- Henriksson, H., Sleeper, M. & Holloszy, J.O. (1987). Reversal of the exercise-induced in muscle permeability to glucose. *American Journal of Physiology, Endocrinology & Metabolism, 235, E331-E335.*

Young, J.H., Gulve, E.A. & Holloszy J.O. (1991) Calcium stimulates glucose transport in Skeletal muscle by a pathway independent of contraction. *American Journal of cell physiology, 260, C55- C561*

Yu, C., Chen, Y. & Cline, G.W. (2002). Mechanisms by which fatty acid inhibits insulin activation of IRS-1 associated phosphatidynositol 3 kinase activity in muscles. *Biological Chemistry, 277, 50230-50236.*

Zalie, A., Moss, S.S., Kniger, H.S. & Van Looyon, J.MJ. (2010).The impact of a 10 week physical activity intervention programme on selective metabolic markers in black adolescents. *South Africa Journal for Research in Sports, Physical Educational & Recreation, 32(1), 147-162.*

Zinman, B. (1990). Diabetes and exercise. *Post-Graduate Medicine; 66, 81-82.*

Zorzano, A., Balon, T.W., Goodman, M.N. & Ruderman, N.B. (1986). Addictive effects of prio exercise and insulin on glucose and AIB uptake by muscles. *American Journal of Physiology, Endocrinology & Metabolism, 251, E21-E26.*