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Research Article

Effect of Swimming Exercise on Levels of Blood Glucose, Adiponectin, Glucose-6-Phosphatase and Lipid Profile in Diabetic Wistar Rats

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Abstract

Diabetes mellitus is a chronic metabolic condition that causes persistent hyperglycemia due to insulin action or secretion. Regular physical exercise has been reported to improve glycemia and lipid profile in diabetes. However, literature is scare on the effects of swimming exercise on the serum levels of adiponectin and glucose 6 phosphatase in Wister rats with diabetes This study therefore, investigated the effects of swimming exercise on adiponectin, glucose 6-phosphatase and lipid profile in male Wistar rats with streptozotocin-induced diabetes. This study was carried out on 25 male Wistar rats grouped into five groups (n=5/group): group 1=control, group 2=diabetes, group 3=diabetes treated with metformin, group 4=non-diabetes and swimming exercise, group 5=diabetes and swimming exercise. Animals in groups 2, 3, and 5 were induced with Streptozotocin (STZ) 50 mg/kg intraperitoneally. After 72 hours of diabetes induction, animals with a blood glucose level of ≥ 200 mg/dl were confirmed diabetics and used for the study. Group 3 animals were treated with metformin 200mg/kg giving orally for 28 days. Animals in groups 4 and 5 were subjected to swimming exercises for 5-10 minutes during the first week until they could swim freely for 30 minutes. The animals were then allowed to swim 5 days per week for 28 days. Swimming exercise for 28 days significantly reduced blood glucose, glucose-6-phosphatase (G6Ppase), Lactate dehydrogenase (LDH), Total cholesterol (TC), and Low-density lipoprotein (LDL) levels but caused significant increase in adiponectin and High-density lipoprotein (HDL) levels in diabetic rats compared with untreated diabetic rats. There was a significant decrease in triglyceride (TG) of diabetic animals caused by swimming for 28 days. This study demonstrated that swimming exercise for 28 days may help lower glucose level and improve insulin sensitivity by increasing adiponectin level and decreasing G6Pase activity in diabetic rats. Also, swimming exercise may help improve lipid profile in diabetic rats.

Keywords

Diabetes, Swimming, Blood Glucose, Lactate Dehydrogenase, Adiponectin, Glucose-6-Phosphatase, Lipid Profile

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic condition that causes persistent hyperglycemia due to insufficient secretion or action of insulin or both [1]. World Health Organization (WHO) projected that population of diabetic patients might reach 300 million in year 2025 [2]. Diabetes is among the ten leading causes of death and disability in United States of America [3]. Lifestyle modifications such as healthy diet, regular exercise, reducing weight, stress management and smoking cessation have

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been reported to play roles in managing, improving health and well-being of diabetic patients [4].

Regular physical activity has been reported effective in preventing and treating some of the risk factors for cardiovascular diseases [5]. It has been shown that physical exercises increased the ability of muscles to burn fat through activation of muscle enzymes involved in lipid metabolism thereby decreasing the TG, TC, LDL, and increasing HDL levels [6, 7]. According to Punthakee et al [8], higher levels of adiponectin during exercise is associated with increase in oxidation of fat and glucose uptake into muscles thereby decreasing complications of type II diabetes mellitus (T2DM).

Swimming is a form of aerobic physical exercise that has been found safe [9]. Swimming exercise is done inside water and involves rhythmic movement done at different levels of intensity or difficulty. According to McNeal [10] factors including water, buoyancy, water pressure, resistance and water temperature are important in swimming. Swimming compared with other exercises does not cause much pressure on the body and reduces the risk of cardiac diseases [11] Regular swimming exercise has been reported to improve risk factors for metabolic syndrome [1]. Flyn et al [12] reported lower glucose level during 45mins of swimming compared to running for the same time. Glucose uptake has been reported higher during incremental swimming test compared to running exercise and that glucose level does not increase at higher intensity steps [13]. Low- intensity swimming exercise training prevented alteration in glycemia, lipid profile, and obesity development induced by neonatal MSG in mice [14]. Swimming has been reported to help with cardiovascular conditioning and toning of body muscles [15].

Dyslipidemia is characterized by high levels of plasma triglycerides (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C), and low levels of high-density lipoprotein cholesterol (HDL-C). Dyslipidemia results in severe diseases like coronary artery disease, myocardial infarction [16]. Previous study showed that swimming reduced TC, TG, LDC-L, and increased HDL-C [17]. Swimming has been reported to significantly improve lipid profile in women [15]. Adiponectin produced by white adipocytes regulates lipid levels, and plays important roles in metabolic function, and inflammation [18]. Adiponectin acts as a link between lipid metabolism and atherosclerosis [19]. It has been reported that adiponectin knock-out animals developed severe dyslipidemia [20, 21]. There is limited information on swimming exercise and the levels of adiponectin and glucose-6-phosphatase in streptozotocin-induced diabetes.

Streptozotocin (STZ) is used to induce experimental diabetes in rodents [22] and capable of causing disruption in the levels of normal glucose homeostasis in rats [23]. STZ is considered the most used diabetogenic compound for inducing diabetes in experimental animal models [24]. Reports have shown that STZ can induce mild to severe diabetes depending on the dose, strain, age of animal, nutritional status and route of administration [24, 25]. This study investigated the effects of swimming exercise on the levels of adiponectin, glucose-6-phosphatase, LDH and lipid profile in STZ-induced diabetes in male Wistar rats.

2. Materials and Methods

25 male Wistar rats weighing between 180-200g were used in the study. Animals were acclimatized for two weeks in a regular habitat under photoperiodic settings (12 hours of light and 12 hours of darkness) and at ambient room temperature of 28 ℃ to 30 ℃.

They had access to grower chow and water. The animals were kept in an animal house in the Department of Physiology, University of Ibadan, Ibadan. All the animals were kept in transparent, sanitary cages with soft wood shaving floors that were changed every other day. The study was conducted in complete conformity with the "Principle of Laboratory Animal Care" and following the University of Ibadan Animal Care and Use Research Ethics Committee (ACUREC) regulations. The Weights of the animals were measured and recorded weekly.

After acclimatization, the animals were grouped into five groups (n=5).

1. Group 1: Control group
2. Group 2: Negative control group (Diabetes group)
3. Group 3: Diabetes treated with Metformin group
4. Group 4: Nondiabetics and swimming exercise group
5. Group 5: Diabetics and swimming exercise group

Following an overnight fast, streptozotocin (50 mg/kg) was injected intraperitoneally into experimental animals to induce diabetes. Streptozotocin (STZ) was freshly prepared in 0.1M citrate buffer (pH 4.5), and control group animals received freshly prepared 0.1M citrate buffer (pH 4.50) only. To prevent hypoglycemia, experimental animals were given unrestricted access to a solution of sucrose (10g/100ml) orally overnight. After 72 hours of diabetes induction, animals with a basal blood glucose level of ≥ 200 mg/dl were classified as diabetics and used for the study. The swimming exercise was performed as described by [26]. The tank was filled with fresh water, and a controlled temperature was used. The diabetic and non-diabetic animals were subjected to swimming exercises 5 days per week for 28 days. In the first week, the animals gradually adapted to swimming by gradually increasing the swimming time from 5 minutes until the animals could swim freely for thirty minutes.

2.1. Preparation of Streptozotocin

Streptozotocin (STZ) is the most used diabetogenic drug for inducing type 1 and type 2 diabetes in rat models [27]. STZ was stored at -20 ℃. STZ is hydrophilic and light-sensitive, so the solution was prepared under low light in batches and used freshly after preparation. The drug was dissolved in sodium citrate buffer (50 mM, pH 4.45).

2.2. Swimming of Animals

The swimming exercise was performed as described by [26]. Group 4 and 5 animals were subjected to swimming exercises five times per week and were allowed two days of rest a week. The animals were made to swim in a tank filled with fresh water at a temperature of 32 ±1 ℃. In the first week, the animals were allowed to swim for five to eight minutes until they could swim for 30 minutes. The swimming exercise was carried out 5 times/week throughout the period of the experiment (28 days).

2.3. Determination of Blood Glucose

Blood glucose was determined using an Accu Check glucometer, which works on the principle of the glucose oxidase method [28]. Blood was collected from the tip of the tail, a drop of blood was put on the glucometer test strip, and the blood glucose value was read from the display screen.

2.4. Estimation of Lactate Dehydrogenase Activity

The LDH was determined using a commercial LDH Fortress Kit from Fortress Diagnostics Limited, United Kingdom. The kit consists of reagent A and reagent B.

2.5. Statistical Analysis

Data were presented as Mean ± SEM of the variables measured. Differences in mean values were compared using student's t test and one-way of variance (ANOVA) followed by Tukey post-hoc test using software Prism, version 9.0.0 (Graph-Pad Software Inc. San Diego, CA. USA). Statistical significance was considered at $p<0.05$ level.

3. Results

The results of the experiments carried out are shown in Figures 1-8. All values given in the graph are mean ±standard error of the mean (SEM), and asterisks in the graph indicate values significantly different from the control of the measured values.

3.1. Effect of Streptozotocin on Blood Glucose

Injection of streptozotocin (50mg/kg) caused a significant increase in blood glucose level of the animals when compared with control animals. However, swimming exercise and metformin caused significant decrease in blood glucose level of diabetic animals when compared with the untreated diabetic group (figure 1).

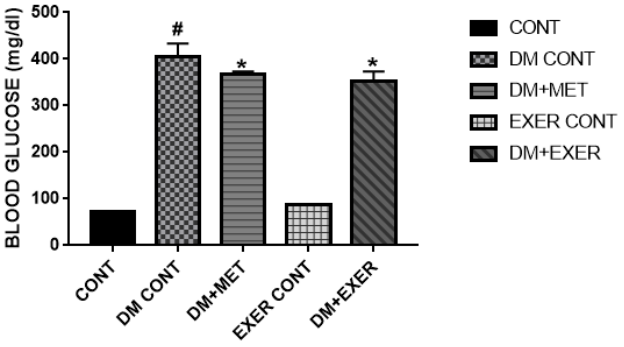

Figure 1. *Effect of streptozotocin on blood glucose level. Values are expressed as mean ±SEM, n=5. # p<0.05 DM CONT vs CONT, *p<0.05, DM+MET, DM+EXER vs DM CONT. STZ injection caused a significant increase in blood glucose levels compared with control group. Treatment with metformin and swimming for 28days caused significant decrease in glucose levels compared with untreated diabetic group.*

3.2. Effect of Swimming Exercise on Adiponectin

Diabetic animals had significant lower adiponectin levels compared with the control group, however treatment with metformin and swimming exercise for 28 days caused significant increase in the levels of adiponectin compared with untreated diabetic animals (figure 2).

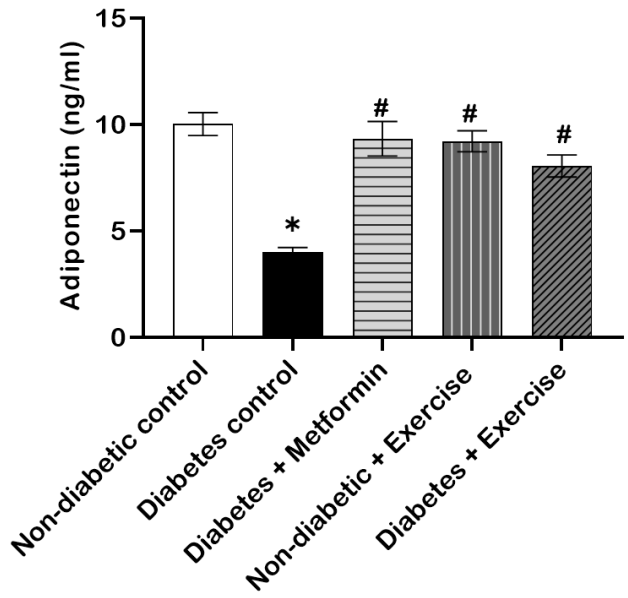

Figure 2. *Effect of swimming exercise on adiponectin levels. Values are expressed as mean ±SEM, n=5. * p<0.05 DM CONT vs CONT, # p<0.05, DM+MET, DM+EXER vs DM CONT. Animals in the swimming and metformin groups had significant increase in adiponectin level compared with untreated diabetic group.*

3.3. Effect of Swimming Exercise on Lactate Dehydrogenase

Injection of streptozotocin (50mg/kg) caused a significant increase in lactate dehydrogenase. However, there was a significant decrease in lactate dehydrogenase levels of the diabetes animal treated with metformin when compared with the untreated diabetic group. There was also a significant decrease in lactate dehydrogenase levels of diabetic animals subjected to swimming exercise when compared with the untreated diabetic group (figure 3).

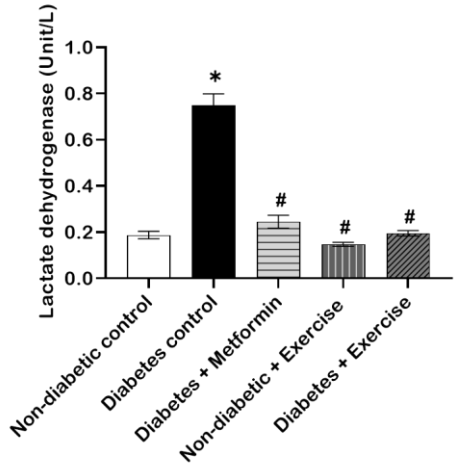

Figure 3. *Effect of swimming exercise on lactate dehydrogenase levels. Values are expressed as mean ±SEM, n=5. * p<0.05 DM CONT vs CONT, # p<0.05, DM+MET, DM+EXER vs DM CONT. STZ injection caused significant increase in LDH level of animals compared with control group. Treatment with metformin and swimming for 28days caused significant decrease in LDH levels compared with untreated diabetic group.*

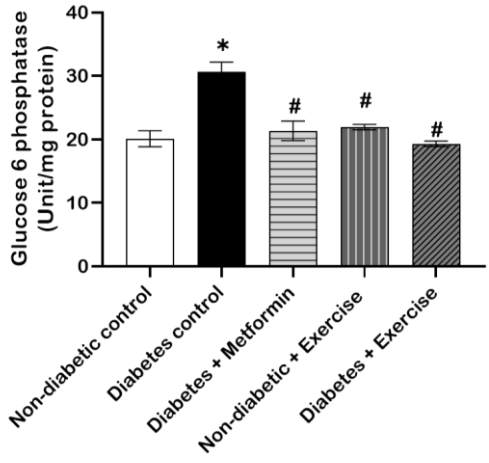

Figure 4. *Effect of swimming exercise on glucose-6-phosphatase levels. Values are expressed as mean ±SEM, n=5. * p<0.05 DM CONT vs CONT, # p<0.05, DM+MET, DM+EXER vs DM CONT. Animals in the swimming and metformin groups had significant decrease glucose 6-phosphate levels compared with untreated diabetic group.*

3.4. Effect of Swimming Exercise on Glucose-6-Phosphatase

There was a significant difference in the level of glucose-6-phosphatase of animals treated with metformin and animals subjected to swimming exercise when compared with the untreated diabetic group (figure 4).

3.5. Effect of Swimming Exercise on Lipid Profile

Figure 5 shows the effect of swimming exercise on total cholesterol levels. There was a significant decrease in total cholesterol levels of diabetic animals subjected to swimming exercise and metformin when compared with the untreated diabetic group.

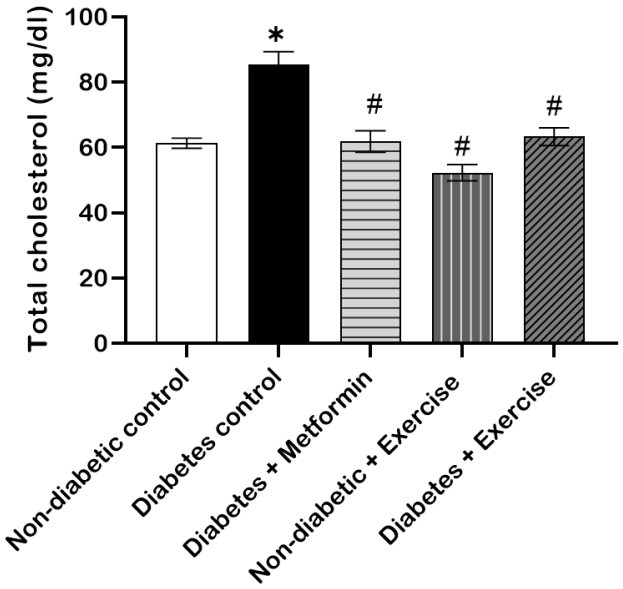

Figure 5. *Effect of swimming exercise on total cholesterol levels. Values are expressed as mean ±SEM, n=5, * p<0.05 DM CONT vs CONT, # p<0.05 DM+MET, DM+EXER vs DM CONT. STZ injection caused significant increase in total cholesterol level compared with control. # p<0.05 DM CONT vs CONT, Animals treated with swimming exercise and metformin had a significant reduction in total cholesterol compared with untreated diabetic animals.*

3.6. Effect of Swimming Exercise on High-Density Lipoprotein

Figure 6 shows the effect of swimming exercise on high-density lipoprotein levels. There was a significant increase e in HDL levels of diabetic animals subjected to swimming exercise and metformin when compared with the untreated diabetic group.

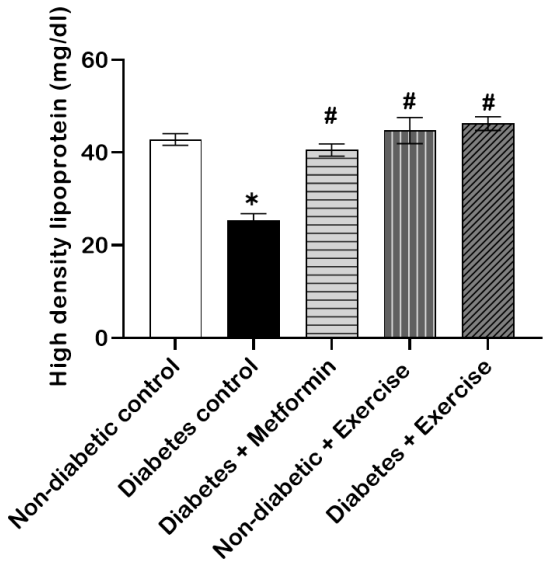

Figure 6. *Effect of swimming exercise on HDL levels. Values are expressed as mean ±SEM, n=5. *p<0.05 DM CONT vs CONT, # p<0.05 DM+MET, DM+EXER vs DM CONT. STZ injection caused a significant decrease in HDL levels compared with control. Animals treated with swimming exercise and metformin had a significant increase in HDL levels compared with untreated diabetic animals.*

3.7. Effect of Swimming Exercise on Low-Density Lipoprotein

Figure 7 shows the effect of swimming exercise on low-density lipoprotein levels. There was a significant decrease in LDL levels of diabetic animals subjected to swimming exercise and metformin when compared with the untreated diabetic group.

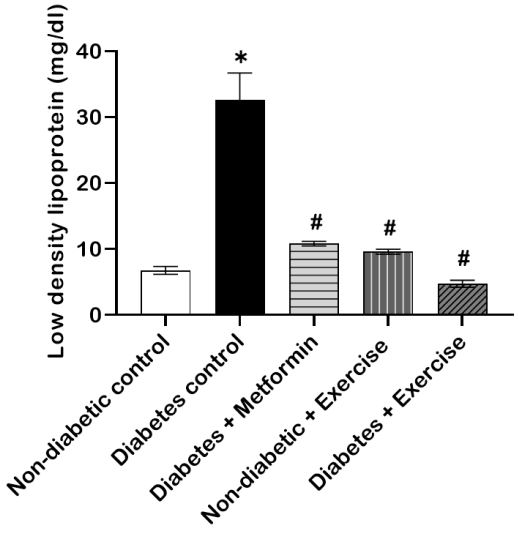

Figure 7. *Effect of swimming exercise on LDL levels. Values are expressed as mean ±SEM, n=5. *p<0.05 DM CONT vs CONT, # p<0.05 DM+MET, DM+EXER vs DM CONT. Animals treated with swimming exercise and metformin had a significant decrease in LDL levels compared with untreated diabetic animals.*

3.8. Effect of Swimming Exercise on Triglyceride

Figure 8 shows the effect of swimming exercise on triglycerides. There was a significant decrease in triglyceride levels of diabetic animals subjected to swimming exercise when compared with the untreated diabetic group.

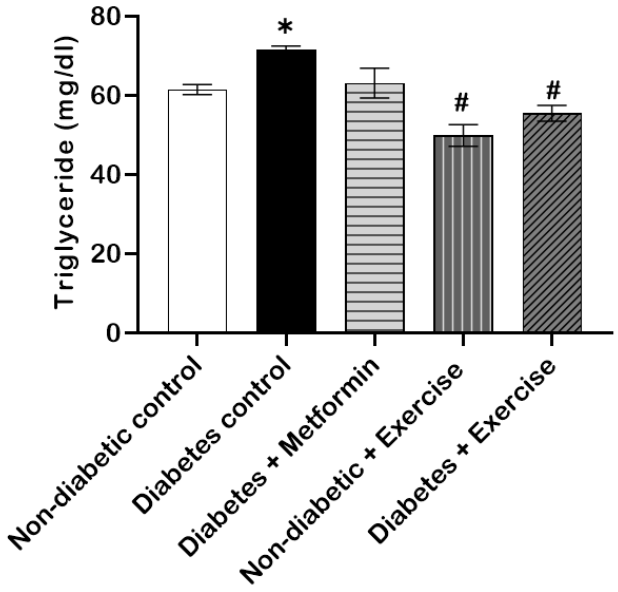

Figure 8. *Effect of swimming exercise on TG levels. Values are expressed as mean ±SEM, n=5. *p<0.05 DM CONT vs CONT, # p<0.05 DM+MET, DM+EXER vs DM CONT. Animals treated with swimming had significantly lower triglyceride levels compared with untreated diabetic animals (DM control group).*

4. Discussion

This study investigated the effects of swimming on serum levels of adiponectin, glucose 6 phosphatase and lipid profiles of ST2 induced diabetic rats. Results show that swimming exercise for 28 days significantly increased adiponectin levels, reduced glucose 6 phosphatase levels, and reduced the level of lactate dehydrogenase activity in ST2 induced diabetic rats. Also, swimming exercise for 28 days reduced total cholesterol, triglycerides, LDL, and increased HDL levels in ST2 induced diabetic rats.

Reports have shown that ST2 can induce mild to severe diabetes in experimental animals depending on the dose, strain, age of animal, nutritional status and route of administration [22, 24, 25] ST2 is also capable of disrupting the levels of normal glucose homeostasis in rats [23].

Adiponectin is derived from adipose tissue and plays an important role in glucose and lipid metabolism. Adiponectin has been reported to suppress hepatic glucose production and improves insulin sensitivity [29]. Adiponectin prevents development of vascular changes and has anti-oxidative and anti-inflammatory effects [30]. The findings of this study in

which diabetic rats had significantly decreased level of adiponectin compared with control is consistent with previous reports [31, 32] Lower serum level of adiponectin is associated with insulin resistance and type 2 diabetes [33, 34] However, swimming exercise and metformin treatment for 28 days in diabetic rats raised the blood levels of adiponectin [35]. High level of adiponectin is associated with improved insulin sensitivity and peripheral glucose uptake [35, 36]. Adiponectin sensitizes body tissues to insulin and there is an inverse relationship between adiponectin, its receptors and insulin resistance [30, 37]. There is a negative correlation between serum adiponectin and hemoglobin A1c (HbA, C)-indicator of glycemic control [37]. The observation of the present study in which swimming exercise for 28 days significantly increased adiponectin level in diabetic rats seems to suggest that swimming exercise may be effective in improving insulin sensitivity thereby regulating glucose levels in diabetes.

Lactate dehydrogenase enzyme (LDH) converts pyruvate to lactate to provide energy during anaerobic glycolysis in cytosol and mitochondria [38] (Bouche et al, 2004). Kavanagh et al [39]. LDH activity is restricted by glucose, insulin and NADH but improved by cytosolic ATP, Ca^{2+} and mitochondrial membrane potential [40]. Reduction in LDH activity may imply that glycolysis produces high ratio of NADH and pyruvate that is oxidized by mitochondria. The observation in this study in which ST2 significantly increased the level of LDH activity in diabetic rats may disrupt beta-cell function reduce insulin sensitivity and disrupts glucose metabolism. This consisted with previous studies [41, 42]. In this study, swimming exercise reduced the activity of LDH, and this may improve glucose (pyruvate) oxidation in the mitochondria.

Glucose-6-phosphatase (G6Pase) is an important enzyme for glucose homeostasis. It is found mainly in the liver and the kidney, important for glucose production during prolong fasting, starvation and diabetes mellitus [38, 43]. In the present study, the significant increase in the G6-pase activity in the liver of diabetic rats compared with non-diabetic control is consistent with previous studies [41, 44]. Metformin treatment and swimming exercise for 28 days however, caused a reduction in the activity of G6Pase of diabetic rats compared with untreated diabetic control animals. Thus, suggesting that swimming exercise may help ameliorate hyperglycemia in diabetes.

The positive effects of swimming exercise on improving lipid profile were also demonstrated in this study. Regular swimming exercise has been reported to have positive impact on TC, HDL, LDL, TG, BMI, and body fat tests [1]. It has also been shown that swimming improved lipid profile especially HDL level in athlete women in academics [15].

5. Conclusion

This study showed that swimming exercise for 28 days was effective in improving insulin sensitivity and ameliorated hyperglycemia in diabetes through activities of adiponectin and glucose 6- phosphatase. Swimming for 28 days also improved lipid profile probably through its effect on adiponectin. This study suggests that swimming exercise may be a non-pharmacological intervention to improving glycaemia and lipid profile in diabetes.

Abbreviations

DM	Diabetes Mellitus
STZ	Streptozotocin
G6Ppase	Glucose-6-Phosphatase
LDH	Lactate Dehydrogenase
TC	Total Cholesterol
LDL	Low-Density Lipoprotein
TG	Triglyceride
HDL	High-Density Lipoprotein
HDL-C	High-Density Lipoprotein Cholesterol
TC	Total Cholesterol
MSG	Monosodium Glutamate
WHO	World Health Organization
T2DM	Type II Diabetes Mellitus
ACUREC	Animal Care and Use Research Ethics Committee

Author Contributions

Isehunwa Grace Olufunmilayo: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Writing – original draft, Writing – review & editing

Layonu Naheemat Mojirade: Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Resources, Visualization

Conflicts of Interest

The authors declare no conflicts of interest.

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