

Effect of *Sesamum indicum* (Linn) Seeds Supplemented Diets on Blood Glucose, Lipid Profiles and Serum Levels of Enzymes in Alloxan Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author HOA designed the study, wrote the protocol and supervised the work. Author ULI carried out all laboratories assays and wrote the first draft of the manuscript. Author IFO performed the statistical analysis and edited the manuscript with author HOA. Author HRA worked on the literature review and references in the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

The present study was aimed at evaluating the effect of *Sesamum indicum* (linn) seeds supplemented diets on blood glucose, lipid profiles and serum enzymes in alloxan induced diabetic rats. Forty male albino Wistar rats were divided into two broad groups based on diet supplementation with raw and roasted *Sesamum indicum*. Each broad group consisted of five sub-groups of four rats (normoglycemic control, diabetic control, standard drug-glibenclamide treated, diabetic rat treated with 10% *Sesamum indicum* supplemented diet and 20% *Sesamum* supplemented diet) for five weeks. Diabetes was induced by a single dose of freshly prepared alloxan (100 mg/kg b.wt) given intraperitoneally. Blood glucose level was monitored using glucometer. Serum lipid profile and serum enzymes were determined using standard spectrophotometric methods. There was a significant ($p < 0.05$) reduction in the blood glucose levels

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of groups fed diets supplemented with raw and roasted sesame seed by about 34.89% and 37.33% respectively when compared to the diabetic control at the end of the experiment. The trend obtained for blood glucose levels was similar with that observed with the serum levels of cholesterol, triglycerides and low density lipoproteins at the same level of significance ($p < 0.05$). The supplemented diets were able to increase the high density lipoprotein that was found to be low in the diabetic rats. The levels of serum enzymes found to be high in the diabetic rats were significantly ($p < 0.05$) decreased at the end of the experiment with the supplemented diets. This study has shown that *Sesamum indicum* (Linn) seed either raw or roasted is capable of lowering the high blood glucose, lipid levels and some serum enzymes derangement observed in diabetes.

Keywords: Alloxan; glibenclamide; sesame seed; diabetes.

1. INTRODUCTION

The scope of medical practice changes as diseases, therapies and prognoses are constantly shifting. One major change in the field of health care is in the treatment of diabetes which is consuming an increasingly large portion of National Health Care expenditures and effort especially in developed countries. It is alarming to note that approximately one-third of cases of diabetes are currently undiagnosed [1].

There are three forms of diabetes namely Type 1, Type 2 and gestational diabetes and they vary in prevalence and age of onset. Studies have shown that Type 1 diabetes account for about 5-10% of diagnosed diabetes while about 90-95% of people with diabetes have Type 2 diabetes and about 3-8% of pregnant women in the United State developed gestational diabetes [2]. Authors suggest that changes in urbanisation and lifestyle in Africa could be driving the overall increase in diabetes prevalence and that the prevalence of undiagnosed may be high in many African countries as against European countries, due to poor awareness and limited screening facilities. This represent a considerable public health challenge and likely increasing economic burden for poorer nations already faced with problems of under-nutrition and communicable diseases such as HIV/AIDS and tuberculosis [2].

Diabetes is now one of the most common non-communicable diseases globally. Symptoms of this disease include polyuria (frequent urination), polydipsia (increase in thirst) and polyphagia (increased hunger). It is one of the leading cause of death in most high-income countries and there is substantial evidence that it is epidemic in many low and middle income countries. Complication from diabetes, such as coronary artery and peripheral vascular diseases, stroke, diabetic neuropathy, amputations, renal failure and blindness are

resulting in increasing disability, reduced life expectancy and numerous health cost for virtually every society. Diabetes is certain to be one of the most challenging health problems in the 21st century. Globally as of 2010, an estimated 285 million people had diabetes, with type 2 making up about 90% of the cases. In 2011 it resulted in 1.4 million deaths worldwide making it the 8th leading cause of death and it is expected to double by 2030 [3].

There are three main approaches currently available for the treatment of diabetes mellitus: via insulin therapy, oral drug therapy and the use of medicinal plants. Medicinal plants are considered to be effective, relatively non-toxic and have vast potentials but are only partly explored by modern methods. Antihyperglycemic activity of plants is mainly due to their ability to restore the function of pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes [4]. Several medicinal plants that have been evaluated experimentally, are in a type-1 diabetes model, but only a few have been shown to be effective hypoglycemic agents in type-2 diabetes patients, such as extracts of *Bridelia ferruginea* Benth [5]. Several plant species having hypoglycemic activity have been reported in literatures. Most of plants contain glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc., that are frequently implicated as having antidiabetic effect [5].

Alkaloids have been reported to decrease blood glucose levels in STZ-induced diabetic rats and also produce a dose-dependent α -amylase and α -glucosidase inhibitory effect [6]. Its cellular mechanism of action is thought to be mediated by an increase in glucose utilization [7]. Acetylenic glucosides (terpene) inhibit the spontaneous development of diabetes in non-obese diabetic (NOD) mice by modulating the

differentiation of T-helper cells [8]. Several flavonoids decrease plasma glucose levels, with direct effects on glucose metabolizing enzymes and expression of the glucose transporter GLUT4 [9]. The presence of aromatic hydroxyl groups in the benzo- γ -pyran structure of flavonoids is associated with its antioxidant properties, particularly its free radical scavenging effects. These properties have been shown to protect pancreatic islet cells from oxidative stress as well as help in the regeneration of β -cells as has been shown with epicatechin found in green tea [10].

A number of drug options are available for treating diabetes such as sulfonylureas, butamides, biguanides, alpha-glucosidase inhibitor and thiazolidinediones. Prolonged use of these drugs cause side effects ranging from metallic taste, nausea, reduce sensitivity, diarrhoea e.t.c. Insulin preparation are been used with a lot of success to control blood glucose levels. Insulin in the form of natural and modified insulin have been used to treat diabetes but limited by its expense, technical know-how and side effects [11].

Dietary management is one of the most effective ways for treating diabetes. The American Diabetes Association (ADA) develops meal plan for diabetic patient depending on the types of diabetes. The therapeutic efficacy of many plants and seeds including *Sesamum indicum* has been described by many researchers [12]. Sesame seed is easily available, affordable and can be cultivated at low cost while the common form of its utilization is by roasting.

Sesamum indicum (Linn) belongs to the family-pedaliaceae, a flowering plant in the genus *Sesamum*. Sesame seeds have long been categorised as traditional health food in India, other East Asian and African countries. Sesame is an important crop in Nigeria agriculture: it is quite extensively cultivated especially in Northern Nigeria. It is found predominantly in Benue, Niger, Nasarawa and Jigawa States. Nigeria is the fifth largest producer of the commodity in the world with an estimated production of 120,000 metric tonnes annually [13]. It is a pharmaceutically important plant which accumulates a variety of secondary metabolites such as phenolic compounds, terpenes and steroids. The presence of these bioactive compounds make them useful for traditional herbal medications [14]. Most pharmacological studies of *Sesamum indicum* seeds is on its anti

tumour effect, benefits in the Parkinson's disease and antihypertensive effect. There is little record in the use of *Sesamum indicum* (Linn) seeds in the management of diabetes. This research therefore evaluates the hypoglycemic and hypolipidemic properties of sesame seeds supplemented diets.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Chemicals

All chemicals were products of BDH Chemicals Limited, Poole, England. Alloxan was a product of Qualikem fine chem. Pvt Ltd, Vadodara, India while glibenclamide a product of Cayman Chemical Company, USA.

2.1.2 Reagents

All reagents used for lipid profiles and liver function tests were products of AGAPE Diagnostics Limited, Switzerland.

2.1.3 Experimental animals

Forty male albino Wistar rats weighing 150-200g were purchased from the Animal Facility Centre, Faculty of Pharmaceutical Sciences, Ahmadu Bello University, Zaria. The Animals were acclimatized under standard laboratory conditions and normal photoperiod for three weeks before the experiment. The animals were housed in standard plastic cages and fed with commercial pelletised feed and water *ad libitum*. Animal care and handling were done according to the ethical guidelines by the Institutional Animal Ethics Committee [15].

2.2 Methods

2.2.1 Sample collection and preparation

Nigerian grown off-white sesame seeds (NCRI-98-60) were purchased from Engr. Kure Ultra-Modern Market Minna, Niger State, Nigeria and identified at the Department of Biological Sciences, Federal University of Technology, Minna, Niger State, Nigeria. Whole seeds were soaked in water (1:5 w/v ratio) followed by washing with water to remove dirt. The seeds were sundried, milled and stored in a glass container and labelled raw sesame. The roasted sesame seed was prepared by placing washed

raw seeds in a dish and roasted at 110°C for 25 minutes using a household toaster oven (Hamilton Brands, Washington, USA). After roasting, the seeds were allowed to cool to ambient temperature, milled and stored in a glass container and labelled roasted sesame.

2.2.2 Raw and roasted sesame seed diet formulation

The raw and roasted sesame seeds were supplemented with commercial pelletized grower feed at varied proportions (10 and 20%). The diets were freely available to the rats throughout the experimental period of five weeks.

2.2.3 Experimental induction of diabetes

Diabetes mellitus was induced by intraperitoneal injection of freshly prepared alloxan (100 mg/kg.b.wt). Aged-matched normal animals that received an injection of an equivalent volume of normal saline comprise the control group. Diabetes was confirmed after 72 hours of administration, rats with a blood glucose level \geq 200mg/dl were considered diabetic [16].

2.2.4 Experimental design

Eighty male albino rats were divided into two broad groups based on raw and roasted sesame seed supplementations. Each broad group contained five sub-groups of four animals each.

- Group 1: Normal control
- Group 2: Diabetic control
- Group 3: Diabetic rats treated with glibenclamide
- Group 4: Diabetic rats fed 10% raw or roasted sesame seeds supplemented diets
- Group 5: Diabetic rats fed 20% raw or roasted sesame seeds supplemented diets

2.2.5 Oral hypoglycaemic drug preparation

About 0.5 mg/kg.b.wt glibenclamide was given orally to the experimental rats in the standard drug group.

2.2.6 Blood sample collection

Blood samples were collected from the tail end of the rats for measuring the fasting blood glucose each week using a glucometer (ACCU-CHEK Active, Model: GC). After five weeks of treatment, the animals were sacrificed and blood samples (5 ml) collected from jugular vein in

syringe and used for the estimation of liver functions and lipid profile tests.

2.3 Biochemical Analyses

2.3.1 Lipid profile

Serum total cholesterol (TC), triglycerides (TGs), Low density lipoprotein (LDL) and High density lipoprotein (HDL) levels were estimated using the commercial kit (AGAPE, Switzerland) [17].

2.3.2 Serum enzymes activities

Aspartate aminotransferase (AST), Alanine aminotransferase (ALT and Alkaline phosphatase (ALP) in serum were estimated using the commercial kit (AGAPE, Switzerland).

2.4 Statistical Analysis

All data were subjected to statistical analysis using SPSS, version 16.0. The means were compared using T-test and the results presented as mean value of four determinations together with the Standard Error of mean (SEM). The statistically significant difference was defined as $p < 0.05$.

3. RESULTS

The levels of blood glucose in the control and the experimental animals are as shown in Figs. 1 and 2 below. It is evident that the blood glucose levels of the control rats remained fairly constant for the period of the experiment (from 80.16 ± 1.35 mg/dl in the first week to 85.79 ± 1.14 mg/dl in the last week). However, a significant ($p < 0.05$) increase in glucose levels (289.48 ± 2.86 to 383.08 ± 3.60 mg/dl) was observed in the diabetic control group. Diets supplemented either with raw or roasted sesame seed progressively lowered the high blood glucose levels resulting from induction of diabetes. The blood glucose in rats fed with 20% raw sesame seed supplementation had their blood glucose reduced by 34.89% (from 281.06 ± 3.34 mg/dL to 182.99 ± 2.88 mg/dL) in the fifth week while those fed with 20% roasted sesame seed supplemented diet had their blood glucose reduced by 37.33% (from 267.32 ± 3.14 to 167.51 ± 3.16 mg/dL). This reduction was significant ($p < 0.05$) when compared with the levels in the diabetic control (383.08 ± 3.60 mg/dL).

The serum total cholesterol (TC), triglycerides (TGs), Low density lipoprotein (LDL) increased while High density lipoprotein (HDL) decreased significantly ($p < 0.05$) in diabetic rats as compared to the control rats (Figs. 3 and 4). The values for TC in the diabetic control was 131.48 ± 0.38 while in the groups fed 10 and 20% raw sesame supplemented diet were 92.23 ± 0.03 and 85.67 ± 1.91 mg/dl respectively. For the TG, the value of 121.42 ± 0.45 mg/dl was obtained in diabetic control and 85.00 ± 0.97 and 77.76 ± 1.15 for 10 and 20% groups fed raw sesame supplemented diet respectively. LDL was also found to be higher in diabetic control (120.47 ± 0.75 mg/dl) than in the experimental groups (114.86 ± 0.69 and 97.10 ± 0.81 mg/dl for 10 and 20% fed groups respectively). The values for TC, TG and LDL observed for the group treated with standard drug were lowered but not significantly ($p > 0.05$) different from those fed either raw or roasted sesame supplemented diets. The opposite of the trend observed for TC, TG and LDL was observed for HDL. In the diabetic control, the HDL level (21.32 ± 0.45 mg/dl) was found to be lower than in the control (53.92 ± 0.83 mg/dl) and in the experimental groups (24.24 ± 0.46 and 28.65 ± 0.34 mg/dl for 10

and 20% fed groups respectively). The supplemented diets with either raw or roasted sesame seeds were able to decrease the TC, TGs, LDL levels that were high in diabetic control and increased the high density lipoprotein that was found to be low in the diabetic rats.

The serum enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT) and Alkaline phosphatase (ALP) levels in diabetic rats (74.10 ± 0.44 , 83.93 ± 0.56 and 82.60 ± 0.97 IU/L respectively) were significantly ($p < 0.05$) higher than those in the non-diabetic control group (39.35 ± 0.57 , 41.38 ± 1.01 and 40.38 ± 0.80 IU/L respectively). After five weeks of the feeding experiment, the enzymes levels in the standard drug treated group (54.37 ± 0.57 , 52.28 ± 0.91 and 57.63 ± 0.46 IU/L respectively), 10% sesame seed supplemented diet (69.00 ± 0.29 , 75.02 ± 0.50 and 71.71 ± 0.55 IU/L) and 20% sesame seed supplemented diet (64.05 ± 0.46 , 68.47 ± 0.61 and 65.99 ± 0.56 IU/L respectively) were found to be significantly ($p < 0.05$) lower compared to the diabetic group (Figs. 5 and 6). Supplementation with either raw or roasted sesame seed was found to have similar effects on all the parameters determined.

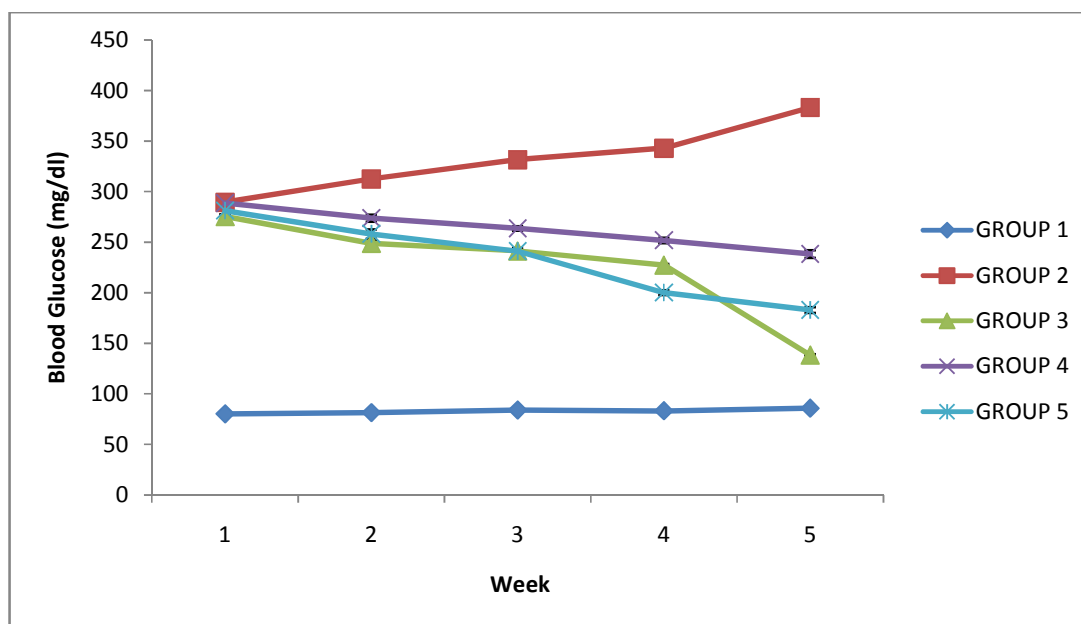


Fig. 1. Effect of diets supplemented with raw sesame seeds on blood glucose levels in diabetic rats

Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with glibenclamide, Group 4: Diabetic rats fed 10% raw sesame seeds supplemented diet and Group 5: Diabetic rats fed 20% raw sesame seeds supplemented diet

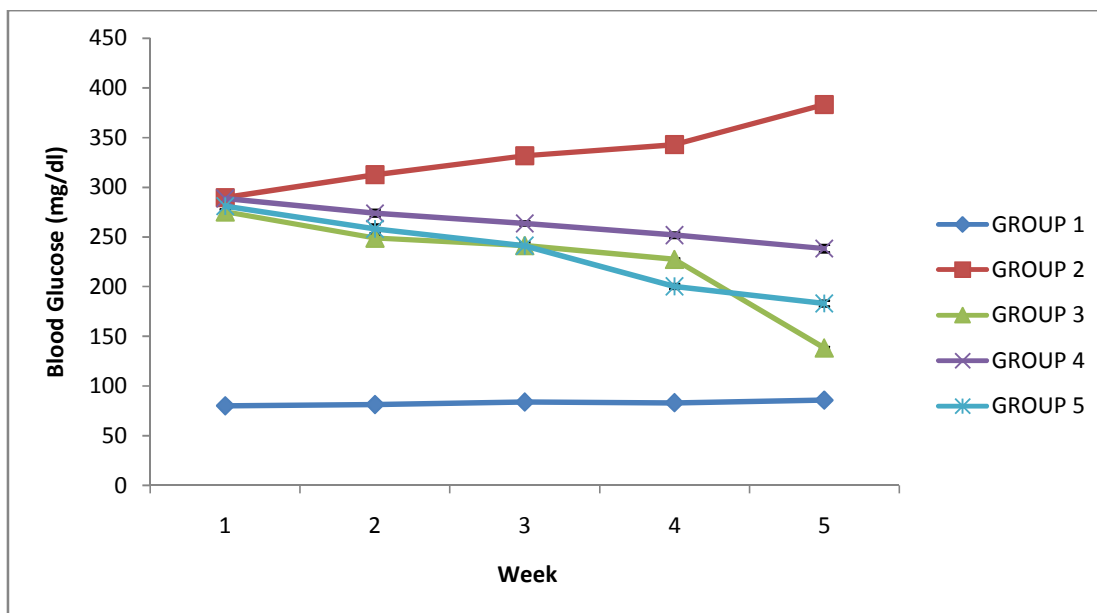


Fig. 2. Effect of diets supplemented roasted sesame seeds on blood glucose levels in diabetic rats

Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with glibenclamide, Group 4: Diabetic rats fed 10% raw sesame seeds supplemented diet and Group 5: Diabetic rats fed 20% raw sesame seeds supplemented diet

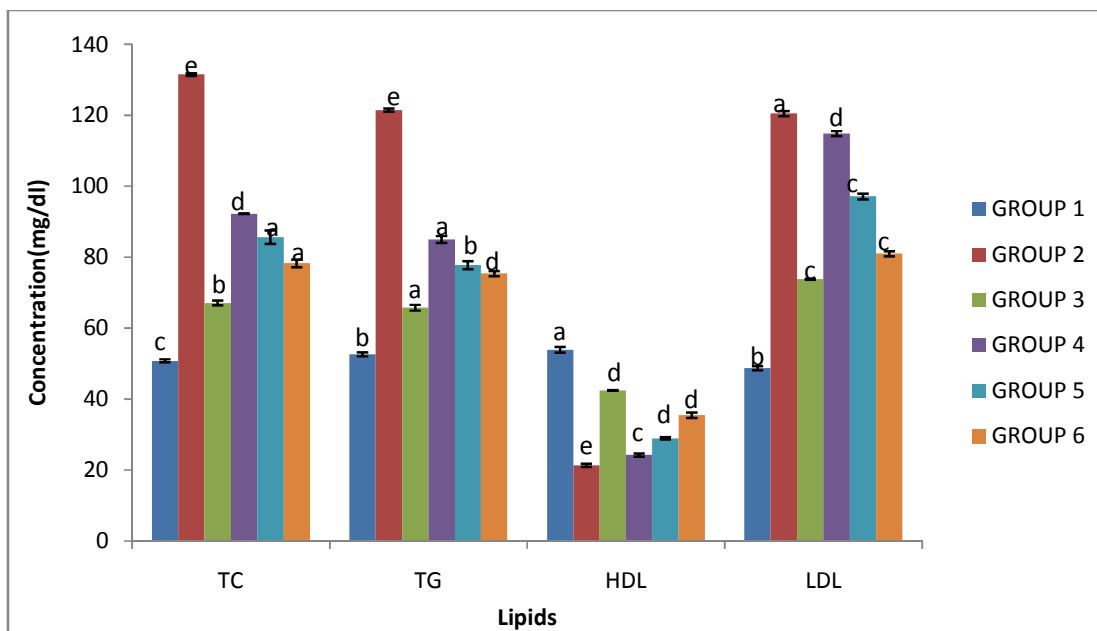


Fig. 3. Effect of diets supplemented of raw sesame seeds on serum lipid profiles in diabetic rats after five weeks of feeding

Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with glibenclamide, Group 4: Diabetic rats fed 10% raw sesame seeds supplemented diet and Group 5: Diabetic rats fed 20% raw sesame seeds supplemented diet

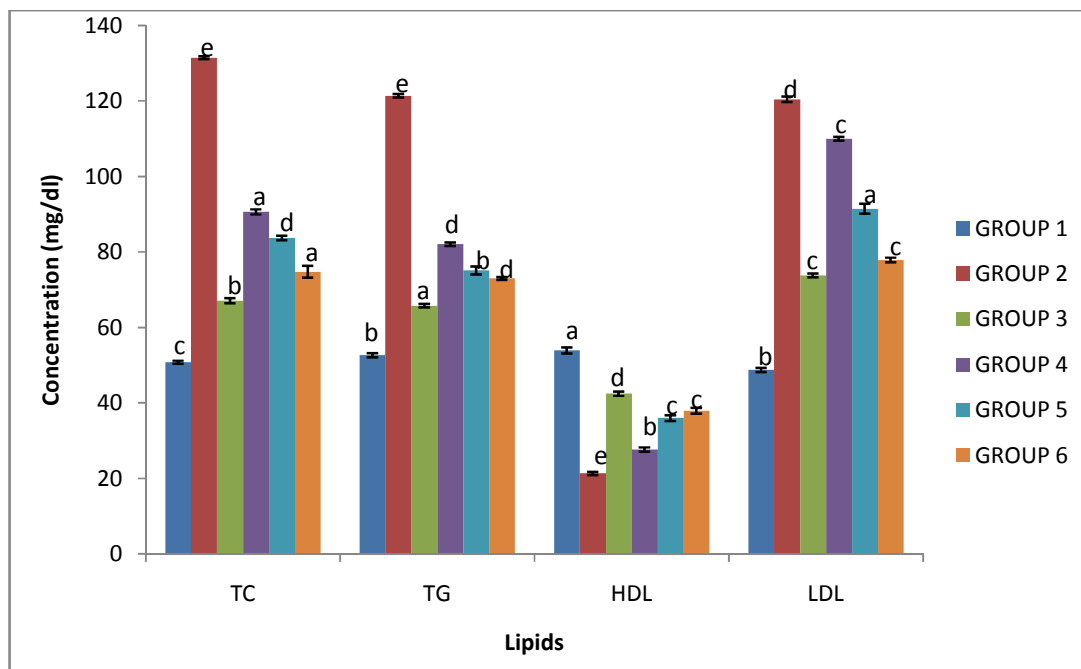


Fig. 4. Effect of diets supplemented with roasted sesame seeds on serum lipid profiles in diabetic rats after five weeks of feeding

Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with glibenclamide, Group 4: Diabetic rats fed 10% raw sesame seeds supplemented diet and Group 5: Diabetic rats fed 20% raw sesame seeds supplemented diet

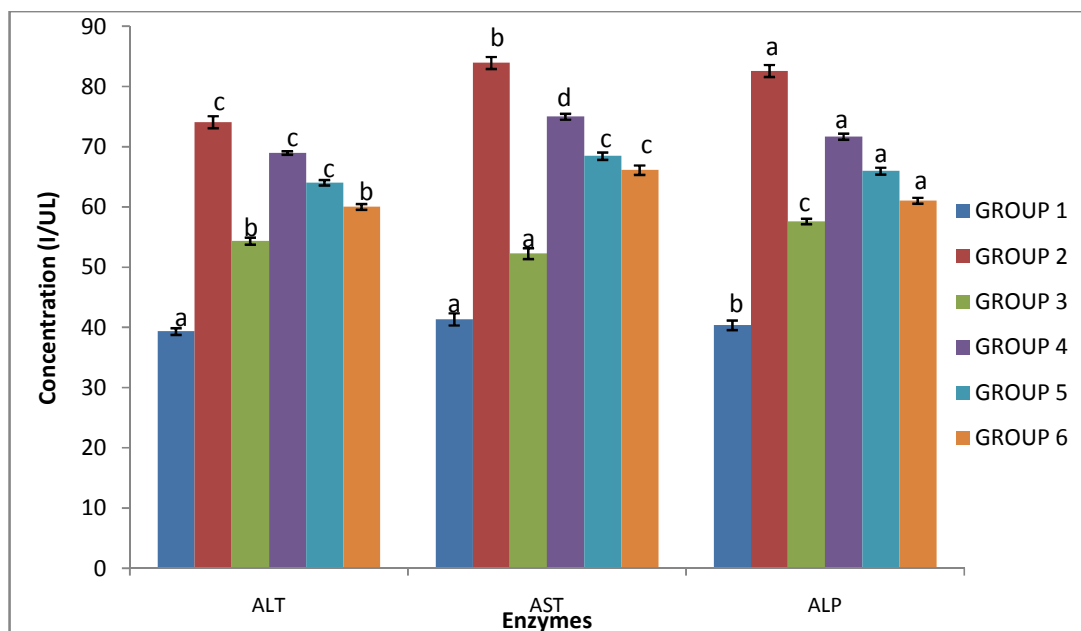


Fig. 5. Effect of diets supplemented with raw sesame on serum enzymes in diabetic rats after five weeks of feeding

Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with glibenclamide, Group 4: Diabetic rats fed 10% raw sesame seeds supplemented diet and Group 5: Diabetic rats fed 20% raw sesame seeds supplemented diet

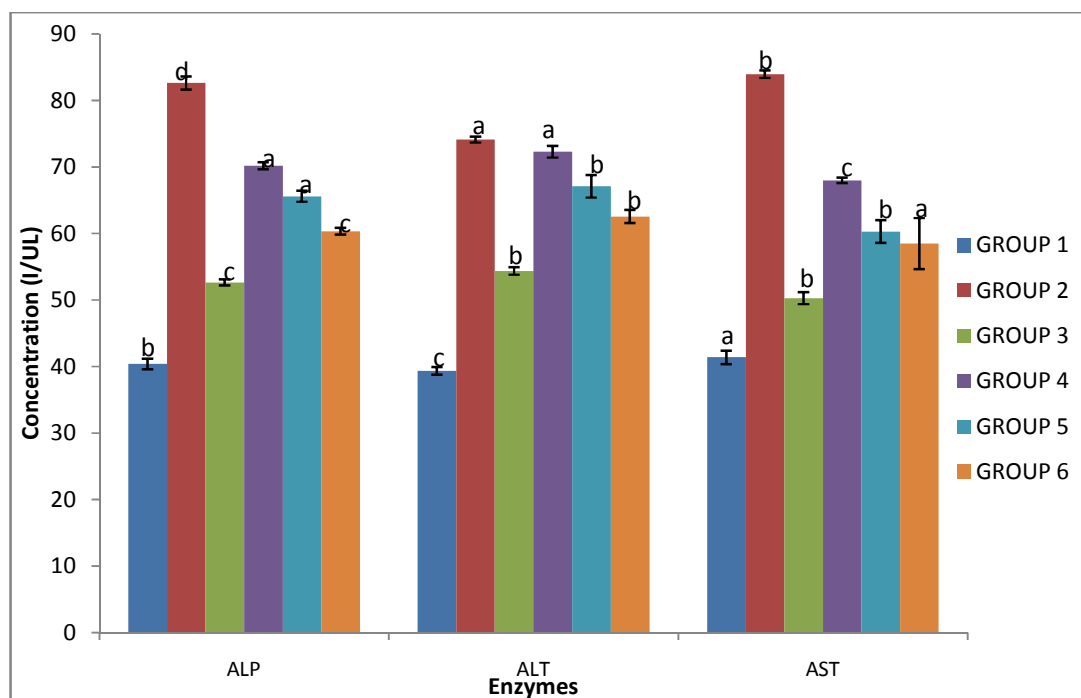


Fig. 6. Effect of diets supplemented with roasted sesame diet on serum enzymes in diabetic rats after five weeks of feeding

Group 1: Normal control, Group 2: Diabetic control, Group 3: Diabetic rats treated with glibenclamide, Group 4: Diabetic rats fed 10% raw sesame seeds supplemented diet and Group 5: Diabetic rats fed 20% raw sesame seeds supplemented diet

4. DISCUSSION

Elevation of blood glucose in rats after induction with alloxan is consistent with literature. Alloxan partially damages selectively the pancreatic insulin secreting β -cells, resulting in a diabetic state and as such has found use in induction of diabetes [18]. The significant reduction of blood glucose levels of the diabetic rats when fed with diets supplemented with *Sesamum indicum* may be explained by the presence of phytochemicals in the seeds. *Sesamum indicum* is found to contain flavonoids, saponins, alkaloids and tannins [19]. Flavonoids are known to have hypoglycemic properties [20]. The reduction in the blood glucose levels by sesame based diet is significantly different from the diabetic control rats but not different from the standard drug (Glibenclamide) treated rats at the end of the experiment (Fifth week). Glibenclamide, an oral hypoglycemic drug generally works by stimulating the pancreas to release more insulin and are only effective when there is some pancreatic beta-cell activity still present [21].

The reduction of blood glucose in the diabetic rats fed with sesame seed based diet may also be due to the presence of sesamin in the seed. Ramesh et al. [20] had reported sesamin to be rich in monounsaturated fatty acid (MUFA). MUFA rich diets have been known to lower blood glucose level. Similar effect have been reported with methanolic and ethanolic extracts of *Azadirachta indica* seed oil in diabetic mice [22] and [23] on the effects of *Parinari Polyandra* seed extract on blood glucose level and other biochemical indices in Wistar Rats.

Lipids play a vital role in the pathogenesis of diabetes mellitus. In diabetes, the increase in blood glucose levels is usually accompanied by an increase in plasma cholesterol (TC), triglycerides (TGs), low density lipoprotein (LDL) and decrease in High density lipoprotein (HDL) [24]. The increased levels of total cholesterol (TC), triglycerides (TG) and low density lipoprotein cholesterol (LDL-C) in the diabetic control rats significantly decreased in the treated rats either with the standard drug, glibenclamide or sesame seed based diets (Figs. 3 and 4) while the opposite was observed for high density

lipoprotein cholesterol (HDL-C). This is in conformity with the report of Ashraduzzaman et al. [25] on the effect of *Vigna inguiculata* seed oil in diabetic rats. It also agrees with the report of Khosla et al. [26] on administration of *fenugreek* seed extract on diabetic rats. It has been suggested that the increase in triglyceride of diabetic animals may be due to insulin deficiency which results in hyperglycemia; fatty acids from adipose tissues are mobilized for energy purpose and excess fatty acids are accumulated in the liver, which are converted to triglyceride [27].

The reduction in cholesterol levels observed in the sesame based diets groups may also be due to the presence of saponins. Saponins have been reported to form complexes with cholesterol and bile acids and prevent them from being absorbed through the small intestine hence lowers the cholesterol level in the blood and liver.

It has also been shown that insulin increases the number of LDL receptors, hence insulin deficiency might be linked to a diminished level of LDL receptor thereby increasing LDL particles resulting in the increase in LDL-cholesterol levels in diabetes [27].

Sesame seed oil has been shown to maintain good cholesterol (HDL) and lowers bad cholesterol (LDL) [28]. Having low HDL levels might results in the risk of developing coronary heart disease especially if other lipids are high such as LDL-cholesterol and triglycerides. Uncontrolled diabetes, being overweight, lack of physical activity and certain medications (anabolic steroids) can also lead to low HDL.

The increase in the activities of serum aspartate aminotransaminase (AST), serum alanine aminotransaminase (ALT) and alkaline phosphatase (ALP) in diabetic rats indicates that diabetes that might have been induced due to liver dysfunction [29] and might have resulted to their leakage from the cytosol of hepatic cells into the blood stream. These enzymes are used as markers in hepatic injury. Supplementation of diets with sesame seeds or treatment with glibenclamide were found to significantly reduce the levels of these enzymes and may be an indication of a reversal of the effects of high blood glucose in the diabetic rats (Figs. 5 and 6) and consequently could alleviate liver damage caused by alloxan. The effect of sesame based diets can be attributed to the presence of sesamin. Sesamin has been known to protect the liver from oxidative damage [28]. Similar effects

have been reported with extracts of *Parinari Polyandra* seed in diabetic rats by [30,23].

5. CONCLUSION

This work has shown that sesame seed diet has the ability to reduce blood glucose, cholesterol, triglycerides, low density lipoproteins and liver function enzymes that are high in diabetes and in addition, able to increase the high density lipoproteins. These properties could be exploited in the management and remedy of diabetes. It is also possible that *Sesame indicum* seed can find use in the management of other related diseases especially those resulting from hyperlipidemia.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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