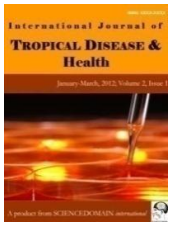

International Journal of TROPICAL DISEASE & Health
5(4): 260-268, 2015, Article no.IJTDH.2015.029
ISSN: 2278–1005

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Serum Lipid Profile of Alloxan-induced Diabetic Rats Fed *Triticum aestivum*-based Diet

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Authors' contributions

This work was carried out in collaboration between all the authors. Also each participated in the concept and design, analysis, data interpretation, writing or revision of this manuscript

Article Information

DOI: 10.9734/IJTDH/2015/12877
Editor(s):
(1) Shankar Srinivasan, Department of Health Informatics, University of Medicine & Dentistry of New Jersey, USA.
Reviewers:
(1) Arun Kumar, Mahavir Cancer Institute & Research Centre, India.
(2) Athanasia Papazafiropoulou, 1rd Department of Internal Medicine, General Hospital of Pireas "Tzaneio", Greece.
Complete Peer review History: http://www.sciencedomain.org/review-history.php?iid=850&id=19&aid=7309

Original Research Article

Received 22nd July 2014
Accepted 14th August 2014
Published 15th December 2014

ABSTRACT

Diabetes mellitus (DM) is a metabolic disorder in which carbohydrate, protein and lipid metabolism is not properly regulated by insulin. Many indigenous medicinal plants have been successfully used to manage diabetes. However, the use of dietary management is most advocated. Thus, the aim of this study was to evaluate the antihyperlipidemic potential of wheat-based diet in alloxan-induced diabetic rats. Forty (40) albino rats (*Rattus norvegicus*) were grouped into four with ten (10) animals in each. Diabetes was induced by the intra-peritoneal injection of alloxan monohydrate (150mg/kg body weight). Group A consists of (non-diabetic) rats fed yam based-diet; group B, (diabetic) rats fed yam flour-based diet and treated with metformin; group C (diabetic) rats fed wheat-based diet while rats in group D (untreated) were fed yam based-diet for four (4) weeks. There was a significant reduction ($p < 0.05$) in the concentration of glucose, triglycerides, cholesterol, LDL cholesterol, VLDL cholesterol and a significant increase ($p < 0.05$) in the level of HDL cholesterol. It is considered that feeding diabetic patient with *Triticum aestivum* (wheat)-based diet would assist in the management of diabetes mellitus.

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Keywords: Albino rats; alloxan; wheat; hyperlipidemia; metformin.

1. INTRODUCTION

Diabetes mellitus (DM) is the most common serious metabolic disorder in the endocrine system and is one of the three causes of death in the world [26,27]. It is a growing health problem in most countries and its incidence is considered to be high all over the world [26,46]. Diabetes mellitus is a mutifactorial disease which generally involves absolute or relative insulin deficiency (type I) and/or insulin resiistance (type II) and ultimately leads to hyperglycemia [26,36]. DM either type I or type II is characterized by hyperglycemia, abnormal lipid and protein metabolism along with specific long–term complications affecting the retina, kidney and nervous system [26]. It is a complex disease associated with myriad of debilitating complications among which cardiovascular diseases are on a resounding note. About 70 to 80% of deaths in diabetic patients are due to vascular diseases [16,43].

Cardiovascular diseases (CVD) contributed to one third of all global death with developing countries**,** low income and middle income countries accounting for 86% of disability-adjusted life years [51]. Some of the risk factors implicated in cardiovascular disease are total plasma cholesterol [30,42], plasma triglycerides [8,47], plasma low density lipoprotein (LDL) cholesterol, plasma very low density lipoprotein (VLDL) cholesterol [1,50], while higher level of high density lipoprotein (HDL) cholesterol play an important role in removing cholesterol from the cells and transport it back to the liver for excretion [2,36].

In addition, the pharmacological currently used for treatment of diabetes (both insulin and biguanides) produce serious side effects [26,43] and fail to significantly alter the course of diabetic complications are not safe for use during pregnancy [26] also the cost of administering these drugs is beyond the reach of people living in the rural area and low income rate people [39].

Although, the uses of herbal drugs has been commonly practiced and considered to be less toxic with fewer side effects [54]. Furthermore, dietary management of diabetes has been believed locally to be helpful and example of such diet is *Triticum aestium (*wheat), *Triticum aestivum* belong to a family Poaceae with *Tritricum species* which is a grass, originally from the Fertile Crescent region of the Near East, but now cultivated worldwide. It has high content of fiber, antioxidant (particularly antioxidant minerals and vitamins) and complex carbohydrate which are believed to exhibit antidiabetic effects [11,31]. The methanolic extract of this plant has been reported by Mohan et al. [31] in the management of diabetic rats. Also, the uses of this plant as a source of diet in diabetes management have been acclaimed without scientific validation. Furthermore, the uses of diets will serve dual roles. Therefore, the aim of this work is to assess the hypolipidemic potential of wheat-based diet in alloxan-induced diabetic rats.

2. MATERIALS AND METHODS

Wheat was obtained from local farmer in Kastina, Kastina State and oven dried at 60°C. *Dioscorea rotundata* (white yam) was used as yam flour (because it is one of the most staple food consumed mainly in the Western Part of Nigeria), obtained from Oja Oba Market in Ilorin, Kwara State, which was peeled, sliced and oven dried (60°C). Soybean and cellulose were also obtained from Oja Oba market in Ilorin, Kwara State. Then each sample was milled separately with local grinding machine. Soybean oil was obtained from Sunola Refined Soybeans, Kewalram Nigeria Limited, and vitamin/mineral mix was obtained from Rofat Feed Nigeria Limited, Ilorin, Kwara State.

Also, alloxan monohydrate (for inducing diabetes) was obtained from Sigma Chemical Company, St Louis Mo U.S.A, while Accu – check active glucometer (for determining the glucose level) was obtained from Roche Diagnostic, Mannheim, Germany.

2.1 Animals and Treatments

A total of 40 male and female albino rats (*Rattus norvegicus*) were used for the experiment with an average weight of 150±20g. They were obtained from the Animal House of the Department of Biochemistry, University of Ilorin, Nigeria.

The animals were kept under standard environmental conditions, with 10 albino rats housed in a cage. All the animals were acclimatized for seven days to the laboratory condition and they received human care accordingly.

2.2 Induction of Diabetes

Alloxan monohydrate of 150 mg/kg bodyweight (dissolved in 0.9% sterile NaCl solution of pH 7) [23,29,38] was administered intraperitoneally to rats in group II to IV to induced diabetes, of which their blood glucose level have been previously determined.

Thereafter, blood was collected from the tail artery of the animals [14] to determine their glucose levels using the Accu-check active glucometer. Rats with serum glucose levels between (250–400 mg/dl), showing clear signs of polyuria, polyphagia and polydipsia after one day were considered diabetic and used for the experiment [19,34].

2.3 Experimental Design

The animal's groups are as follows:

Group A: Non-diabetic rats fed with yam flour-based diet
Group B: Diabetic rats fed with yam flour-based diet plus metformin
Group C: Diabetic rats fed with wheat-based diet
Group D: Untreated diabetic rats fed with yam flour-based diet

The various diets were compounded as shown in (Table 1). The diet and water (*ad libitum)* were given to the appropriate animals in their respective groups.

The animals were fed for 4 weeks and blood glucose level was monitored on every two day. At the end of the feeding period the animals were sacrificed using diethyl ether as anesthesia and blood samples were collected from each animal for serum (in clean sample tubes) parameters analyses. The method of Akanji [3] was employed for serum preparation.

2.4 Parameters Studied

Proximate, minerals, vitamins and amino acid profile of the formulated diets were determined using Association of Analytical Chemist (AOAC) [53]. *In vitro* antioxidants such as DPPH, nitric oxide, ferric reducing power (FRAP), Fe^{2+} chelation, total phenol and total flavonoid were determined using [15,24,32,40,41,45,45] method respectively. Cholesterol, High density lipoprotein cholesterol (HDL-c) and triglycerides were determined by enzymatic method using Randox kits. Low density lipoprotein cholesterol (LDL- c) and very low density lipoprotein cholesterol (VLDL- c) were obtained by deduction using Friedwald equation [20].

2.5 Statistical Analysis

The data were analyzed using one-way ANOVA. Level of significance was assessed using Duncan Multiple Range Test (DMRT) at $p<0.05$ (SPSS 14.0 software was used for data analyses).

3. RESULTS

Tables 2, 3, 4, 5 and 6 show the results of proximate analysis, *in-vitro* antioxidant, mineral analysis, vitamins and amino acids compositions of the formulated diets respectively. There were significant increase ($p<0.05$) in crude fibre, soluble fibre, insoluble fibre, protein (Table 2), DDPH, NO, iron chelation, total flavonoid, total phenol, ferric reducing power (Table 3), zinc, selenium, copper (Table 4), antioxidant vitamins such as vitamins A, C, E (Table 5), seventeen amino acids (including essential and glucogenic amino acids) (Table 6) ($p<0.05$) in wheat-based diet (Feed B) when compared with control diet (Feed A), while there were no significant difference ($p>0.05$) in the moisture contents of Feed A and B (Table 1). The results of the lipid

Table 1. Diets composition of various groups (g/100)

Ingredient	Group A	Group B	Group C	Group D
Wheat	-	-	57.6	-
Yam flour	57.6	-	-	57.6
Yam flour + metformin	-	57.6	-	-
Soyabeans	25	25	25	25
Soyabeans oil	6	6	6	6
Cellulose	6	6	6	6
D-methionine	0.4	0.4	0.4	0.4
Vitamin/mineral	5	5	5	5

profile indicated that alloxan administration significantly increased ($p<0.05$) total cholesterol, triglyceride, VLDL and LDL levels above the normal control value with significant reduction ($p<0.05$) in HDL levels (Fig. 1). Treatment with wheat-based diet reduces the abnormal increased in total cholesterol, very low density lipoprotein (VLDL) and low density lipoprotein (LDL) with significant increase ($p<0.05$) in the high density lipoprotein (HDL) levels when compared with the normal group and metformin treated group. Also, Fig. 2 shows the result of fasting blood glucose levels, with highest levels ($p<0.05$) in diabetic control group, which was reduced to minimal level when treated with wheat based-diet and metformin.

Table 2. Percentage proximate analysis of the formulated diets

Parameters (%)	Feed A	Feed B
Ash	2.39±0.15[a]	5.59±0.55[b]
Lipid content	6.50±0.12[a]	8.44±1.12[b]
Protein	16.89±0.07[a]	20.63±0.03[b]
Moisture content	1.56±0.39[a]	1.75±0.02[a]
Fibre	8.39±0.04[a]	16.62±0.01[b]
*Insoluble dietary fiber	6.39±0.05[a]	12.34±0.01[b]
*Soluble dietary fiber	2.00±0.02[a]	4.28±0.02[b]
Carbohydrate (by different)	64.27±0.35[a]	46.97±0.45[b]

Each value is a mean of three determinations±SEM, Values with different superscripts across the row are significantly different (p<0.05); Legend; Feed A = yam flours based-diet, B = wheat based-diet

Table 3. *In-vitro* antioxidant parameters of the formulated diets

Parameters	Feed A	Feed B
DPPH	23 .01±0.02[a]	40.00±0.02[b]
Nitric Oxide	2.34±0.03[a]	6.12±0.06[b]
FRAP	0.68±0.09[a]	6.89±0.04[b]
Fe^{+2} chelation	34.23±0.03[a]	58.77±0.02[b]
Total phenol	1.99±0.2[a]	2.38±0.2[b]
Total flavonoid	2.84±0.02[a]	3.34±0.02[b]

Each value is a mean of three determinations ± SEM, Values with different superscripts across the row are significantly different (p<0.05); Legend Feed A = yam flours based-diet, B = wheat based-diet

Table 4. Minerals composition of the formulated diets

Minerals	Feed A	Feed B
Na	248.21±0.02[a]	979.10±0.22[b]
Ca	1.32±0.02[a]	4.83±1.02[b]
Mg	38.96±0.32[a]	87.56±1.22[b]
Zn	10.21±0.02[a]	26.05±0.08[b]
Se	0.21±0.32[a]	1.46±1.02[b]
P	134.05±0.02[a]	176.01±0.02[b]
Fe	1.02±0.42[a]	14.36±0.02[b]

Each value is a mean of three determinations ± SEM, Values with different superscripts across the row are significantly different (p<0.05) Legend Feed A = yam flours based-diet, B = wheat based-diet

Table 5. Vitamins composition of the formulated diet

Vitamins	Feed A	Feed B
A	28.32±0.09[a]	492.11±0.01[b]
D	8.32±0.09[a]	27.69±1.02[b]
E	0.11 ±0.08[a]	9.80±0.01[b]
K	0.09±0.02[a]	0.16±0.02[b]
C	0.94±0.32[a]	15.76±0.01[b]

Each value is a mean of three determinations ±SEM, Values with different superscripts across the row are significantly different (p<0.05); Legend; Feed A = yam flours based-diet, B = wheat based-diet

4. DISCUSSION

Diabetes mellitus remains the most common chronic disorder of carbohydrate, fat and protein metabolism. It is characterized by chronic and persistent hyperglycemia, degenerative vascular changes and neuropathy due to complete or partial insulin secretion or insulin resistance [33]. Moreover, diabetes mellitus is accompanied by hypercholesterolemia, hyperlipidemia and hepatic steatosis [25]. The hypercholesterolemia is a consequence of accelerated fatty acid oxidation to acetyl CoA which is the primary substrate for cholesterol synthesis [50]. Similarly, the hyperlipidemia associated with diabetes mellitus results from accelerated *de novo* hepatic biosynthesis and release of VLDLc without a corresponding increase in the rate of clearance from the blood by the lipoprotein lipase whose activity is dependent on high insulin: glucagon ratio [25].

Table 6. Amino acids composition of the formulated diets

Amino acids	Feed A	Feed B
*Glycine	1.89 ±0.01[a]	4.20±0.32[b]
*Alanine	3.24±1.02[b]	6.98±1.08[b]
*Serine	3.21±0.12a	5.20±0.12[b]
*Proline	3.82±1.00[a]	5.54±0.15[b]
*#Valine	2.96±1.02[a]	5.32±0.05[b]
*#Threonine	1.48±0.22[a]	3.69±0.05[b]
#Isoleucine	2.40±0.12[a]	3.96±0.05[b]
#Leucine	4.90±1.02[a]	11.52±0.05[b]
*Aspartate	5.20±0.02[a]	9.92±0.05[b]
#Lysine	2.20±0.02[a]	7.35±1.02[b]
*#Methione	1.20±2.02[a]	1.49±0.02[b]
*Glutamate	12.20±2.02[a]	19.48±1.02[b]
#Phenylalanine	4.20±0.02[a]	8.39±1.03[b]
*#Histidine	2.22±0.02[a]	3.40 ±0.02[b]
#*Arginine	3.27±1.12[a]	6.92±1.02[b]
*Tyrosine	1.01±1.02[a]	2.24 ±1.02[b]
*cysteine	1.16±1.02[a]	1.24±1.14[b]

*Each value is a mean of three determinations ± SEM, Values with different superscripts across the row are significantly different (p<0.05) Legend Feed A = yam flours based-diet, B = wheat based-diet, * = glucogenic amino acids; #= essential amino acids*

Metformin, a prototype of the second generation sulfonyurea class of the oral hypoglycemic agents, is known to mediate its hypoglycemic effect by stimulating insulin release from the pancreatic β cells, reducing hepatic insulin clearance, stimulating the release of somatostatin and suppressing the secretion of glucagon [18]. Sulfonyureas have also been shown to suppress hepatic gluconeogenesis [12].

In the present study, there were abnormal increased in all the serum lipid profiles studied as shown in diabetic control group except in HDL (which was significantly reduced in concentration) when compared with diets treated groups (Fig. 1). But comparing the results of yam flour based-diet plus metformin with those obtained in wheat based-diet. It appears that the latter may be eliciting its normoglycemic effect through enhancement of peripheral glucose utilization [6]. The observed significant reduction in the serum concentrations of triglycerides, total cholesterol and cholesterol fractions could also be due to depressed hepatic gluconeogenesis by wheat based-diet. It may also due to the fact that wheat based-diet significantly elevated the activity of hepatic cholesterol 7-alpha-hydroxylase which is a rate-limiting enzyme in the biosynthesis of the bile acids and stimulates the conversion of cholesterol to bile acids leading to the excretion of cholesterol from the body [35]. Furthermore, it may also due to the inhibition of fatty acid synthesis [17], enhanced excretion or lowered absorption of cholesterol [48] although this claim remains a speculation until it is subjected to further scientific validation by the key enzymes regulating this pathway. A positive relationship between gluconeogenesis and lipogenesis has been well documented in literature [25]. The bioactive compounds (total phenol, total flavonoid, DPPH, Fe^{2+} chelation etc.) and antioxidant substances (selenium, zinc, vitamin A, C, E etc) present in the wheat based-diet may be responsible for the hypolipidemia potential of the diet by reversing the effects of alloxan on the pancreas [7,10,11]. Also the present of glycine, methionine, cysteine in the diets may be responsible for detoxification of reactive oxygen species, produced by alloxan induction [35]. In addition, the present of both soluble and insoluble dietary fibre in the diet may also responsible for lowering rate of bad cholesterol, by retarding the absorption of cholesterol [35].

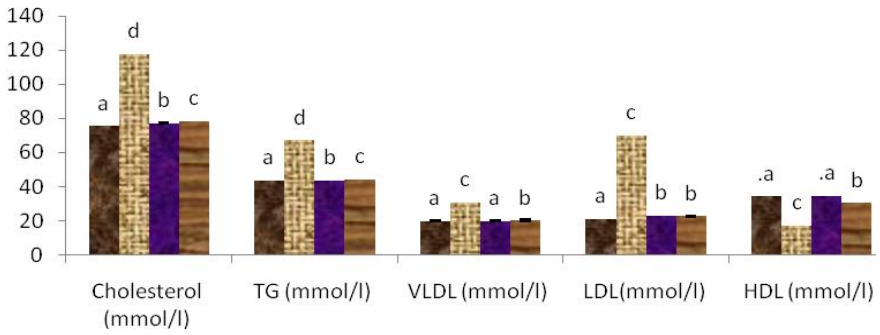

Fig. 1. Effect of formulated diets on lipid profile of alloxan-induced diabetic rats

Each value was mean ± SEM of 10 rats in each group. Values with different superscripts letter (such a, b, c and d) differ significantly (p<0.05). Legend: WD = wheat-based diet

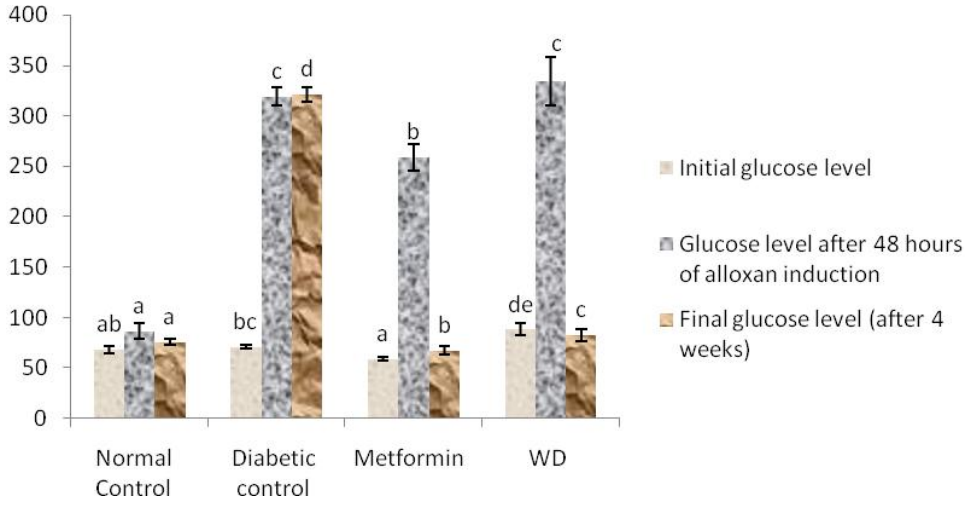

Fig. 2. Effect of formulated diets on serum glucose of alloxan-induced diabetic rats
Each value was mean ± SEM of 10 rats in each group. Values with different superscripts letter differ significantly (p<0.05), Legend: WD = wheat based-diet

Also, there was significant reduction in fasting blood glucose levels of wheat based-diet (Fig. 2) when compared with diabetic control group as shown in Fig. 2. This normoglycemic effect of wheat based-diet (Fig. 2) may due to insulin release from pancreatic cells of diabetic rats, improving insulin action and binding [28], increasing glucose metabolism [13], and high level of soluble and insoluble fiber which interfere with carbohydrate absorption, makes the stomach full and retard the absorption of glucose from gastrointestinal tract [37]. This may be attributed to the present of immune system booster antioxidant vitamins and minerals which have the potential to scavenge reactive oxygen species produced by alloxan induction coupled with glucogenic amino acids in the wheat based –diet [5].

5. CONCLUSION

The study clearly demonstrated that wheat based-diet have antihyperlipidemia potential which may make it highly useful in the management of type II diabetes.

CONSENT

Not applicable.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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