Original Article

Effects of Antioxidant-rich nutraceutical on Selected Metabolic Syndrome Markers in high-fat diet-induced metabolic dysfunction in rat dams and their offspring

*[1]Yusuf, R. S., [2]Isa, S. A., [2]Saidu, Y., [3]Abubakar, M. B. and [4]Wali, U.

[1]Department of Biochemistry, Bauchi State University, Bauchi Nigeria
[1]Department of Biochemistry, Usmanu Danfodiyo University, Sokoto Nigeria
[3]Department of Physiology, College of Health Science, Usmanu Danfodiyo University, Sokoto Nigeria
[4]Department of Chemical Pathology, School of Medical Laboratory, Usmanu Danfodiyo University, Sokoto Nigeria

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ABSTRACT

Metabolic syndrome (MetS) is described based on the disorders of glucose metabolism, hypertension, obesity and dyslipidaemia. MetS can be programmed epigenetically, in later adult life during intrauterine life. This work investigated the modulatory effect of an antioxidant-rich nutraceutical on the processes that predispose foetus to MetS using rats fed high fat diet (HFD). The nutraceutical was prepared from onions, tomato, garlic, ginger, lemon juice, watermelon seed and palm oil in the ratio of 4:4:4:4:2:1:1 respectively while HFD was prepared with rat-chow containing 52 % beef-tallow. Female rats were grouped into two of normal and HFD treated, each of which is further sub-grouped into nutraceutical-supplemented and non-nutraceutical-supplemented. They were allowed to mate with males, conceived and gave birth. Blood samples were collected from the dams and analysed for some biochemical indices. The pups of dams fed normal diet were grouped just like their dams i.e pups fed normal diet only; HFD only; normal diet and nutraceutical and HFD and nutraceutical. Fasting blood glucose, fasting plasma insulin and HOMA-IR were increased in dams fed HFD. Antioxidant enzymes CAT, SOD and GPx were decreased in dams fed HFD while a decrease in oxidative stress marker NO was observed and an increase in MDA. Serum TAG, serum TAG, TChol, LDL and AI were all increased in dams fed HFD only. All these parameters were corrected in dams that were given nutraceutical such that there was no significant difference ($p<0.05$) between their values and those fed normal diet. The results for the pups fed normal diet and whose dams were fed HFD had significantly higher ($p<0.05$) levels of FBG, FPI, HOMA-IR and MDA. NO levels were not significantly different ($p<0.05$) across all groups. TChol, TAG, LDL-C and AI were all increased ($p<0.05$) in pups that had dams that were fed HFD but their levels were decreased ($p<0.05$) in those whose dams were supplemented with the anitioxidant rich nutraceutical. The antioxidant-rich nutraceutical might have conferred protection from the various MetS parameters that were programmed in later adult life of pups whose dams were fed HFD.

Keywords: Metabolic syndrome, Nutraceutical, High-fat Diet, Fetal Programming, Biochemical Indices.

***Correspondence author's email**: ruqayyahsyusuf@sazu.edu.ng

INTRODUCTION

Metabolic syndrome is defined as a worldwide public health issue due to the clinical, metabolic, biochemical, and other correlated changes that it implies, along with the concomitant presence of several pathological conditions, which include the following: abdominal adiposity, hypertension, dyslipidemia, and insulin resistance [1]. The syndrome is characterized by the presence of several interconnected risk factors for type 2 diabetes (T2DM) and cardiovascular disease (CVD)[2]. The incidence of metabolic syndrome increases the risk of developing T2DM by 5-fold, CVD by 2-fold, and the risk of all-cause mortality by 1.5 fold [3]. In excess of an impact of lifestyle, the lack of or presence of physical activity, and a balanced diet of macronutrients and micronutrients, metabolic syndrome is also affected by an individual's predisposition to diseases [4]. Normally programmed development of an individual is usually coordinated by the genetic makeup at conception [4]. For many years, it has been known that some specific environmental factors throughout gestation (e.g., maternal nutrition, maternal lifestyle, metabolic diseases) may cause changes in gene expression and permanently damage the structure and function of some specific organs of the fetus. Therefore, many non-communicable diseases such as obesity, cardiovascular disease, diabetes, hypertension, kidney disease, allergic disease, nonalcoholic fatty liver disease, neurocognitive impairments, and metabolic syndrome may occur later in life [5].

The term "nutraceutical" was coined as a combination of nutrition and pharmaceutical, and it refers to any substance that may be considered a food or component of a food that offers medical or health benefits [6]. A growing body of evidence indicates that nutraceuticals have a broad range of beneficial effects on human health. These include protection against cardiovascular diseases, diabetes, obesity, stress, and other diseases [7]. Research from our laboratory has shown that antioxidant rich nutraceutical lowered the blood pressure and glucose level and may have promising effect in the prevention and management of cardiovascular complications of hypertension and diabetes [8]. Therefore, the present study aimed to investigate the development of metabolic dysfunction and the potential beneficial effects of antioxidant-rich nutraceuticals in high-fat diet-induced metabolic dysfunction in rat dams and their offspring.

MATERIALS AND METHODS

Chemicals and reagents

All the chemicals and reagents used in this study were of analytical grade. Superoxide dismutase, Catalase, Glutathione peroxide, Malondialdehyde, Insulin and Nitric oxide ELISA kits were all products of Nanjing Pars Biochem Co. Ltd. China, while the Lipid profile kits (Total cholesterol, HDL-c and TG) assay kits were products of Agappe Diagnostics Switzerland GmbH.

Formulation of high fat diet (HFD)

The HFD was formulated in accordance with Kim *et al.* with some modifications [9]. The formulation consists of 46% of fat from beef tallow, 24% of carbohydrate, 20.3% of protein, 5% of fibre, salt mixture of 3.7% and vitamins mixture 1%.

Nutraceutical formulations

The nutraceutical was prepared according to the method of [8]. It was compounded locally using the following ingredients: tomato, onion, garlic, ginger, lemon, melon seed and palm oil, in a ratio of 4:4:4:4:2:1:1. The wet ingredients were dried at a temperature of 40°C. This was done by mixing 20 g of onions; 20 g of garlic, 20 g of tomatoes and 20 g of ginger in 100 ml distilled water and blended using electric blender. Exactly, 10 g of ground water melon seeds were then added and blended once again. To this, 5 g of lemon juice and 5 g of palm oil were added, mixed. The nutraceutical was then spread on a clean flat surface and allowed to dry at room temperature and stored in airtight containers until required.

Experimental Animals

The study was conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals, and all experimental protocols and procedures were approved by the Central University Ethics Committee and also in compliance with Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines on animal research. Wistar rats of both sexes weighing between (140 g -170 g) were used for research. The animals were purchased from the Department of Biological Science, Usmanu Danfodiyo University, Sokoto, Nigeria and the experiment took place in the animal house, Faculty of Pharmaceutical Sciences, Usmanu Danfodiyo University Teaching Hospital (UDUTH). The animals were kept in plastic cages surrounded with metallic net to prevent rats from escaping under a 12 hour light/dark cycle, with room temperature in the range of 28°C-30°C and given standard rat chow (where applicable) (Chikun Growers' mesh) and were allowed access to clean water *ad libitum* before and during the experimental period.

Animal Grouping and Treatment

The nutraceuticals were administered (where applicable) by intubation using syringe and plastic canular. The experiment was carried out in 2 phases: Phase 1- Six female rats were mated with males in a ratio of 2 females to 1 male in each group. When pregnancy was confirmed, the male rats were evacuated and the female rats were either given normal diet (ND) only (Group A), ND and NT (Group B), HFD only (Group C) and HFD and NT (Group D). They were fed till they gave birth and weaned their pups. The pups were separated from the dams after weaning and the pups obtained from the group fed normal chow were fed as above with those fed ND (Group A1), ND and NT (Group B1), HFD only (Group C1) and HFD and NT (Group D1) (five animals per group). Rat dams were anaesthetized under chloroform vapour and their blood samples collected via heart puncture. Also, after feeding and treatment for a duration of 10 weeks, the pups were also anaesthetized under chloroform vapour and their blood samples collected via heart puncture. Sera was obtained from the various blood samples by centrifuging the clotted blood samples at 4000g and were stored at – 80^{o}C until needed.

RESULTS

Effect of antioxidant-rich nutraceutical supplementation on fasting blood glucose, fasting plasma insulin and Homeostasis Model Assessment of insulin resistance (HOMA-IR) of dams fed HFD

The effect of antioxidant-rich nutraceutical supplementation on fasting blood glucose, fasting plasma insulin and HOMA-IR of dams fed HFD are presented in Table 1. The result showed a significant increase ($p < 0.05$) in fasting blood glucose in HFD fed rats compared to control. Plasma insulin was also significantly higher ($p < 0.05$) in HFD fed rat compared to control. Also, the same pattern of increase was observed in HOMA-IR compared to control. Equally, fasting blood glucose, fasting plasma insulin and HOMA-IR in dams that were given both HFD and nutraceutical supplementation, were not significantly different from those of the normal control

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Table 1: Effect of antioxidant nutraceutical supplementation on glucose, insulin and HOMA-IR of dams fed HFD

GROUP	FBG (mmol/L)	FPI (mU/L)	HOMA-IR
A	5.24 ± 0.27^{a}	35.11 ± 1.55^{b}	8.18 ± 1.55^{b}
B	6.23 ± 0.13^{b}	79.57 ± 4.09^{c}	22.03 ± 4.09^{c}
C	5.03 ± 0.15^{a}	23.00 ± 1.32^{a}	5.14 ± 0.76^{a}
D	5.73 ± 0.03^{a}	35.09 ± 3.12^{b}	8.94 ± 3.16^{b}

FBG-fasting blood glucose; FPI-fasting plasma insulin; HOMA-IR-Homeostasis Model Assessment of insulin resistance. Group A (Control)- fed standard chow only; Group B -fed High Fat Diet (HFD) only; Group C- fed normal diet and 250 mg/kg nutraceutical; Group D - HFD and 250 mg/kg nutraceutical Data was analyzed using one way ANOVA followed by Post hoc Duncan multiple comparison test. Values are expressed as Mean $\pm$ SEM; n=5/group.
Values with different superscripts on the same column are significantly different ($p < 0.05$).

Effect of antioxidant-rich nutraceutical supplementation on antioxidant enzymes in dams fed HFD

The activities of cellular antioxidant enzymes catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPX) were assessed and the data presented in Table 2. In this study, CAT activity was significantly ($p < 0.05$) decreased in HFD fed rats compared to the control group. However, CAT activity was significantly restored by supplementation with antioxidant nutraceutical in the HFD supplemented with nutraceutical group compared to HFD fed only group. SOD activity was also significantly ($p < 0.05$) decreased in HFD fed rats compared to the control group. The activity of SOD was significantly restored by supplementation with antioxidant nutraceutical in the HFD supplemented with nutraceutical group compared to HFD fed only group. GPx activity was also significantly ($p < 0.05$) decreased in HFD fed rats compared to the control group. Increase in GPx activity was however observed by supplementation with antioxidant nutraceutical in the HFD supplemented with nutraceutical group compared to HFD fed only group.

Table 2: Effect of antioxidant-rich nutraceutical supplementation on level of antioxidant enzymes in dams fed HFD

GROUP	CAT (ng/L)	SOD (ng/L)	GPX (nmol/L)
A	39.87 ± 1.54^{b}	110.59 ± 3.65^{c}	88.71 ± 7.41^{bc}
B	19.05 ± 0.55^{a}	14.73 ± 2.02^{a}	42.96 ± 4.84^{a}
C	43.39 ± 4.22^{b}	105.76 ± 8.90^{c}	118.04 ± 20.94^{c}
D	36.83 ± 1.63^{b}	48.96 ± 1.63^{b}	54.62 ± 0.76^{ab}

CAT-catalase, SOD-superoxide dismutase, GPX-glutathione peroxidase, Group A-fed with standard chow only (normal control), Group B- fed with HFD only, Group C fed with normal diet and 250 mg/kg of nutraceutical, Group D- fed with HFD and 250 mg/kg nutraceutical. Data was analyzed using one way ANOVA followed by Post hoc Duncan multiple comparison test. Values are expressed as Mean ± SEM; n=5/group. Values with different superscripts on the same column are significantly different ($p < 0.05$).

Effect of antioxidant-rich nutraceutical supplementation on the levels of oxidative stress markers in dams fed HFD

Nitirc oxide (NO) and malondialdehyde (MDA) concentrations are two important markers of oxidative stress. MDA formation in different groups is shown in Figure 1. Rat dams fed HFD only had significant increase in lipid peroxidation indicator (MDA) ($p < 0.05$) compared to control group. Antioxidant nutraceutical supplementation prevented the lipid peroxidation in HFD fed rats (Figure 1). The result of the NO was presented in Figure 1. NO concentrations in Rat dams fed HFD only significantly decrease ($p < 0.05$) compared to control group. Antioxidant nutraceutical supplementation restored NO concentration to near normal (Figure 1).

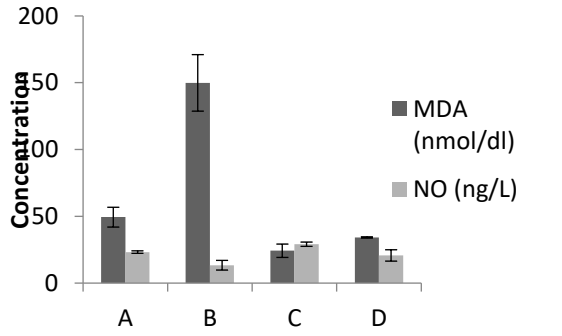

Figure 1: Effect of antioxidant-rich nutraceutical supplementation on oxidative stress markers in dams fed HFD

MDA-Malondialdehyde; NO- Nitric oxide; Group A- fed with standard chow only (normal control), Group B- fed with HFD only, Group C fed with normal diet and 250mg/kg of nutraceutical, Group D- fed with HFD and 250 mg/kg nutraceutical. Data was analyzed using one way ANOVA followed by Post hoc Duncan multiple comparison test. Values are expressed as Mean ± SEM; n=5/group. Values with different superscripts on the same column are significantly different ($p < 0.05$).

Effect of antioxidant-rich nutraceutical supplementation on lipid profile and atherogenic index of dams fed HFD

The lipid profile in the serum of HFD fed rats were measured to evaluate the lipid-lowering effect of antioxidant nutraceutical supplementation on HFD fed rats. The results of the lipid profiles of the rats are presented in Table 3. In the study, serum triglyceride and total cholesterol levels were significantly increased ($p < 0.05$) in rats that were fed HFD compared to the control rats. Antioxidant nutraceutical supplementation significantly ($p < 0.05$) reduced the serum triglyceride and total cholesterol levels in HFD fed rats ($p < 0.05$). Furthermore, the low-density lipoprotein (LDL) cholesterol level was also significantly increased ($p < 0.05$) in HFD fed rats compared to the control rats. Antioxidant supplementation significantly ($p < 0.05$) decreased the plasma LDL cholesterol level in HFD fed rats. However, the lipid profiles of control rats supplemented with antioxidant nutraceutical did not change considerably compared to control. Atherogenic index (AI) of the group fed with HFD was observed to be significantly increased ($p < 0.05$) when compared with control. However, AI values were not significantly different between HFD supplemented and normal supplemented groups

. Table 3: Effect of antioxidant nutraceutical supplementation on lipid profile of dams fed HFD

GROUP	T.CHOL (mg/dL)	TAG (mg/dL)	HDL-c (mg/dL)	LDL-c (mg/dL)	VLDL-c (mg/dL)	AI
A	161.26±10.78^{a}	89.67±7.62^{a}	42.33±6.33^{ab}	101.00±9.78^{a}	17.93±1.08^{b}	2.39±0.06^{b}
B	284.67±13.35^{c}	156.33±5.82^{a}	25.67±5.36^{a}	227.73±8.68^{b}	31.27±1.80^{d}	8.87±0.64^{d}
C	144.13±4.21^{a}	84.00±6.03^{b}	76.00±24.01^{b}	51.33±6.21^{a}	16.80±2.41^{a}	0.68±0.19^{a}
D	181.60±8.17^{b}	151.67±21.96^{a}	49.67±6.89^{ab}	101.59±8.27^{ab}	30.33±2.82^{c}	2.05±0.45^{c}

T.CHOL-total cholesterol, TAG-triacylglycerol, HDL-c-high density lipoprotein cholesterol, LDL-c- low density lipoprotein cholesterol, VLDL-c- very low density lipoprotein cholesterol. Group A- fed with standard chow only (normal control), Group B- fed with HFD only, Group C fed with normal diet and 250 mg/kg of nutraceutical, Group D- fed with HFD and 250mg/kg nutraceutical. Data was analysed using one-way ANOVA followed by Post hoc Duncan multiple comparison test. Values are expressed as Mean ± SEM; n=5/group. Values with different superscripts on the same column are significantly different ($p < 0.05$).

Effect of antioxidant-rich nutraceutical supplementation on fasting blood glucose, fasting plasma insulin and HOMA-IR of pups from dams fed HFD

The effect of antioxidant-rich nutraceutical supplementation on fasting blood glucose, fasting plasma insulin and HOMA-IR of pups from dams fed HFD was presented in Table 4. The result showed a significant increase ($p < 0.05$) in fasting blood glucose in pups of HFD fed rats compared to control. Plasma insulin was also significantly higher in pups of HFD fed rat compared to control. However, the same pattern of increase was also observed in HOMA-IR compared to control.

Table 4: Effect of antioxidant-rich nutraceutical supplementation on the fasting blood glucose, insulin and HOMA-IR of pups fed normal diet

GROUP	**FBG (mmol/L)**	**FPI (mU/L)**	**HOMA-IR**
A1	4. 99± 0.22^{g}	33.12±6.65^{cd}	7.36± 2.17^{de}
B1	5. 93 ± 0.22^{a}	40.22±3.34^{bc}	10.62±0.45^{abcd}
C1	4.67± 0.37^{cde}	32.66±3.37^{ab}	6.78 ± 1.45^{abcd}
D1	5.67±0.09^{bcd}	34.32±4.34^{a}	8.67±1.13^{abcd}

FBG-fasting blood glucose, FPI-fasting plasma insulin, HOMA-IR-Homeostasis Model Assessment of insulin resistance; A1-pups fed standard chow from dams fed standard chow; B1- pups fed standard chow from dams fed HFD; C1- pups fed normal diet from dams fed normal diet and 250 mg/kg nutraceutical, D1- pups fed normal diet from dams fed HFD and 250 mg/kg nutraceutical. Values are expressed as Mean ± SEM; n=5/group. Values with different superscripts are significantly different ($p < 0.05$).

Effect of antioxidant-rich nutraceutical supplementation on antioxidant enzymes in pups of dams fed HFD

The activities of cellular antioxidant enzymes catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GPX) in pups were assessed and the data presented in table 5. Pups whose parents were fed HFD only showed significantly low levels of catalase, superoxide dismutase and glutathione peroxidase ($p < 0.05$) when compared with pups from dams fed normal standard chow. The activity of these enzymes was significantly ($p < 0.05$) higher in pups of dams supplemented with antioxidant nutraceutical compared to pups from HFD fed only.

Table 5: Effect of antioxidant-rich nutraceutical supplementation on level of antioxidant enzymes in pups of dams fed HFD

GROUP	CAT (ng/L)	SOD (ng/L)	GPx (nmol/L)
A1	30.56 ± 2.65^{cd}	62.80 ± 1.49^{b}	73.18 ± 5.54^{c}
B1	22.37 ± 1.07^{b}	37.85 ± 4.30^{b}	49.10 ± 7.82^{a}
C1	37.51 ± 2.18^{ef}	65.74 ± 4.72^{ef}	63.36 ± 4.38^{a}
D1	43.48 ± 3.33^{g}	55.64 ± 9.15^{g}	57.22 ± 5.32^{g}

CAT-catalase, SOD-superoxide dismutase, GPX-glutathione peroxidase; A1-pups fed standard chow from dams fed standard chow; B1- pups fed standard chow from dams fed HFD; C1- pups fed standard chow from dams fed normal diet and 250 mg/kg nutraceutical, D1- pups fed standard chow from dams fed HFD and 250 mg/kg nutraceutical. Values are expressed as Mean ± SEM; n=5/group. Values with different superscripts are significantly different ($p < 0.05$).

Effect of antioxidant-rich nutraceutical supplementation on the levels of oxidative stress markers in pups of dams fed HFD

Nitric oxide (NO) and malondialdehyde (MDA) concentrations are two important markers of oxidative stress. NO and MDA levels of the pups are shown in Figure 2. Pups from dams fed HFD only had significant increase in lipid peroxidation indicator (MDA) ($p < 0.05$) compared to those whose dams were fed normal diet. Antioxidant nutraceutical supplementation in dams prevented the lipid peroxidation in pups of dams fed HFD supplemented groups (Figure 2). However, in no significant difference ($p < 0.05$) of NO was observed across all the groups in pups (Figure 2).

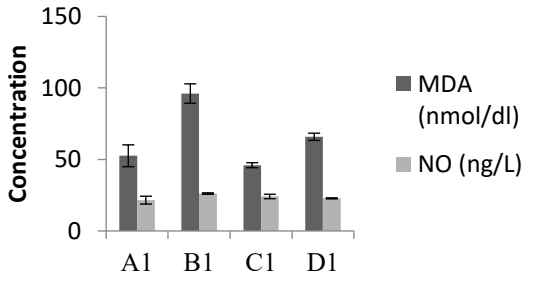

Figure 2: Effect of antioxidant-rich nutraceutical supplementation on the levels of oxidative stress markers in pups of dams fed HFD

MDA-Malandialdehyde; NO- Nitric oxide; A1-pups fed standard chow from dams fed standard chow; B1- pups fed standard chow from dams fed HFD; C1- pups fed standard chow from dams fed normal diet and 250 mg/kg nutraceutical, D1- pups fed standard chow from dams fed HFD and 250 mg/kg nutraceutical. Values are expressed as mean ± SEM. n=5/group.

Effect of antioxidant-rich nutraceutical supplementation on lipid profile and atherogenic index of pups of dams fed HFD

Lipid profile in the serum of pups from HFD fed dams was measured. The results of the lipid profiles of the rats were presented in Table 6. In the present study, serum triglyceride and total cholesterol levels were significantly increased ($p < 0.05$) in pups of rats that were fed HFD compared to the control rats. Antioxidant nutraceutical supplementation significantly ($p < 0.05$) reduced the serum triglyceride and total cholesterol levels in pups of HFD fed rat dams ($p < 0.05$). Furthermore, low density lipoprotein (LDL) cholesterol level was also significantly increased ($p < 0.05$) in pups of HFD fed rats compared to the control rats. Antioxidant supplementation significantly ($p < 0.05$) decreased the plasma LDL cholesterol level in pups of HFD fed rats. Atherogenic index (AI) of the pups from dams fed with HFD was observed to be significantly higher compared ($p < 0.05$) when compared with control

. Table 6. Effect of antioxidant-rich nutraceutical supplementation on the lipid profile of pups fed normal diet

GROUP	TCHOL (mg/dL)	TAG (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)	AI
A1	74.67 ± 1.20^{b}	48.67 ± 4.63^{bcd}	29.33 ± 3.38^{b}	35.60 ± 3.69^{ab}	9.73 ± 0.32^{ab}	1.17 ± 0.87^{a}
B1	107.55 ± 5.24^{c}	59.33 ± 3.93^{def}	22.15 ± 3.33^{b}	73.53 ± 7.76^{cd}	11.87 ± 0.72^{cd}	3.33 ± 0.45^{b}
C1	69.00 ± 3.05^{a}	47.00 ± 2.31^{ab}	33.33 ± 2.91^{b}	26.27 ± 4.21^{a}	9.40 ± 0.32^{a}	0.83 ± 0.19^{a}
D1	92.20 ± 5.78^{c}	51.00 ± 4.00^{bc}	27.33 ± 5.21^{b}	54.67 ± 8.78^{de}	10.20 ± 0.87^{de}	2.00 ± 0.37^{a}

T.CHOL-total cholesterol, TAG-triacylglycerol, HDL-c-high density lipoprotein cholesterol, LDL-c- low density lipoprotein cholesterol, VLDL-c- very low density lipoprotein cholesterol, AI-atherogenic index. A1-pups fed standard chow from dams fed standard chow; B1- pups fed standard chow from dams fed HFD; C1- pups fed normal diet from dams fed normal diet and 250 mg/kg nutraceutical, D1- pups fed normal diet from dams fed HFD and 250 mg/kg nutraceutical. Values are expressed as Mean $\pm$ SEM; n=5/group. Values with different superscripts are significantly different ($p < 0.05$).

DISCUSSION

Several studies have shown the global rise in the prevalence of metabolic syndrome despite recent advances in medicine. Conversely, gestational exposure to various stimuli has also shown to have effect on physiology and metabolism of organisms later in life. Consumption of high fat and high energy diet impairs fetal development leading to long term effects on offspring [10]. Effects of maternal HFD exposure can be passed on to generations, and as such health effects of HFD maternal exposure on generations contribute to the increased rates of metabolic disorders [11].

Continuous feeding with HFD in rat dams was associated with various components of metabolic syndrome, suggesting that HFD feeding used in this study can induce metabolic dysfunction in rat dams. Rat dams fed HFD showed increased body weight gain compared to normal diet. This is due to the fact that HFD contains high calorie and fat content but with low protein contents. Low protein content, as a result of maternal protein restriction during pregnancy has been shown to induce metabolic dysfunction in both dams and their offspring [12].

HFD fed rats showed an increased body weight gain compared to the control. Rats fed HFD supplemented with nutraceutical showed decrease final body weight compared to HFD fed only rats. The average gestation period in all groups was not significantly different. HFD has been used in animal models to induce obesity and has been an important model to study the disruption of body metabolism. The animal models, mostly rats and mice display an increase in body weight and other dyslipidemic changes [13].

Maternal supplementation with various forms of nutrients may have beneficial effects on the metabolic outcome of the offspring in adult life [7]. The use of natural antioxidant nutrients in the prevention and management of metabolic disorders has been reported by several researchers [14]. Several advantages are attached to the use of these natural antioxidant nutrients which include availability, cost effectiveness and lack of adverse effects. In the present study, antioxidant rich nutraceutical was formulated and its effects in HFD-induced metabolic dysfunction were evaluated in rat dams and their offspring.

Studies have shown that HFD feeding increases fasting blood glucose levels due to increase in hepatic glucose

concentration [15]. Our findings indicated significant increase in FBG and insulin levels in HFD rats. More so, similar pattern of increases was also observed in pups of dams fed HFD. Nutraceuticals have been shown to improve glycemic control, insulin sensitivity, and oxidative stress in patients with metabolic dysfunctions [16]. This is in agreement with our findings in which nutraceutical supplementation prevented the increase in glucose levels and insulin, thereby decreasing the risk of developing metabolic dysfunction.

Catalase, SOD and GPx are produced naturally in the body and are responsible for reducing the detrimental effect of oxidative stress. Studies have shown that HFD compromised the activities of these cellular antioxidants [17]. In this study, HFD feeding in dams was observed to cause oxidative stress as evident by alterations in the levels of antioxidant enzymes SOD, catalase and GPx. In the offspring of HFD fed group, SOD, catalase and GPx were also significantly altered. These results agree with previous studies that show compromise in antioxidant defenses as a result of HFD feeding [17]. The antioxidant effect exerted by the nutraceutical formulation could partly be due to the presence of antioxidant compounds such phenolic compounds, carotenoids, vitamins and minerals [18, 19]. We hypothesized that HFD feeding is associated with upregulation of genes involved in ROS production, oxidative damage and subsequent disruption of glucose homeostasis (as evident in the result of fasting blood glucose, fasting plasma insulin and HOMA-IR, leading to metabolic dysfunction. Thus, this study found beneficial effects of supplementation with antioxidant rich nutraceuticals in ameliorating HFD induced oxidative stress.

Nitric oxide and Malondialdehyde are two important markers of oxidative stress and studies have established a link between levels of NO and metabolic disorders and cardiovascular risk [20]. We observed that HFD feeding decreased circulating levels of NO. ROS production during oxidative stress have been shown to reduce the bioavailability of NO due to its inactivation by superoxide anion radical [21]. HFD feeding significantly increased circulating levels of MDA compared to groups fed normal feed or supplemented with nutraceutical.

Hyperlipidemia is associated with a group of metabolic disorders characterized by elevated levels of lipids in the body. Maternal HFD has been shown to cause metabolic changes in fetal adipose tissue, resulting in alteration of fetal growth and development [22]. In this study, HFD feeding resulted in increased serum levels of T.Chol, TAG and LDL-C, VLDL-C and low levels of HDL-C. Similarly, pups from dams fed HFD showed similar pattern of increase compared to control. These results agree with previous studies[23]. Meanwhile, serum levels of TChol, TAG and LDL-C and VLDL-C were significantly low in groups supplemented with antioxidant nutraceutical compared to HFD group. These results suggest the hypolipidemic property of the antioxidant nutraceutical. Dams fed HFD also showed high AI value, while groups supplemented with antioxidant nutraceutical have significantly lower AI values. AI is an important indicator of higher risk for developing atherosclerosis cardiovascular disorders [23, 24].

CONCLUSION

In conclusion, the present study demonstrated that antioxidant rich nutraceutical is effective in reducing body weight, serum glucose, oxidative stress and total cholesterol and triacylglycerol in HFD fed rats. There was significant increase in oxidative stress in offspring of HFD fed rats. Maternal supplementation with antioxidant rich nutraceutical during pregnancy decreased both maternal and offspring oxidative stress. The potential mechanism for the rich antioxidant nutraceutical mediated beneficial effects observed may include decrease inflammation and lipid accumulation and increase in antioxidant defense systems. Thus, collectively the data indicate the usefulness of antioxidant nutraceuticals in relation to poor fetal nutrition in developmental programming of metabolic disorders.

Author Contribution

YUSUF R. S., ISA S. A., SAIDU Y. , ABUBAKAR M. B. and WALI U. designed the experimental work and YUSUF R. S carried out the animal studies as well as statistical analysis of the data obtained from the study. ISA S. A., SAIDU Y. , ABUBAKAR M. B. and WALI U. supervised the experimental progress. YUSUF R. S. drafted the original manuscript while all supervisory team was involved in the proofreading and correction of the original manuscript.

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Conflict of interest

The authors declare no conflict of interest in this work

Informed consent

Informed consent was sought from all researchers that took part in the study.

Ethical approval

The study was conducted in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and all experimental protocols and procedures were approved by the Central University Ethics Committee and also in compliance with ARRIVE guidelines on animal research

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