

***Brassica oleracea* (cabbage)-based diet ameliorates high fat diet-induced hyperlipidaemia in rats**

H. O. B. Oloyede,¹ G. O. Aina,*¹ M. O. Salawu,² T. O. Ajiboye,¹ A. T. Oladiji,¹ M. T. Yakubu,¹ M. O. Nafiu,

*Corresponding Author: musasalawu@yahoo.com ,
salawu.mo@unilorin.edu.ng
Tel: +2348056168553

1. Department of Biochemistry, University of Ilorin, Ilorin 240001, Nigeria
2. Antioxidants, Free Radicals, Functional Foods and Toxicology Research Laboratory, Department of Biological Sciences, Al-Hikmah University, Ilorin 230236, Nigeria.

Abstract

Hyperlipidaemia is a metabolic disorder characterised by alterations in serum lipid profile. It has been well established that nutrition plays an important role in the aetiology of hyperlipidaemia and atherosclerosis. The ameliorative effect of *Brassica oleracea* (cabbage)-based-diet on high fat diet-induced hyperlipidaemia in albino rats was investigated in this study. Twenty-four albino rats were grouped into six of four animals per group. Group 1 (control) was fed with isocaloric feed. Group 2 animals were fed with high-fat diet (HFD). Group 3 was fed with high-fat diet for the eight weeks but treated with atorvastatin from week 5 to week 8 (RFD). Groups 4, 5 and 6 were first fed with the high-fat diet for the first four weeks after which their diets were switched to 10%, 25% and 50% cabbage-based diets (CBD) respectively. The results showed that animals in group 2 exhibited significantly ($p < 0.05$) higher levels of blood lipids and elevated heart and liver disease parameters. Antioxidants enzymes activities were also reduced and lipid peroxidation significantly elevated in this group. Group 3 animals (RFD) showed significantly ($p < 0.05$) reduced lipid peroxidation and serum cholesterol levels while aspartate transaminase (AST), alanine aminotransferase (ALT) and creatine kinase activities were not significantly different from the control in the heart, but AST and ALT activities in the liver significantly elevated ($p < 0.05$). Groups 4, 5 and 6 animals showed

significantly reduced ($p < 0.05$) level of serum cholesterol and AST, ALT, creatine kinase (CK), atherogenic index (AI) and CHD risk reductions which were dependent on the cabbage content of the diets. Lipid peroxidation was also significantly reduced ($p < 0.05$) in these groups. From this study we conclude cabbage-based diets were able to ameliorate hyperlipidaemia and lipid peroxidation and thus maintained the integrity of the membranes of the liver and heart of rats exposed to diet-induced hyperlipidaemia.

Keywords: Hyperlipidaemia, diet-induced, high-fat diet, cabbage-based diet, atherosclerosis, dietary fibres.

Background

Hyperlipidaemia, is a disorder characterized by abnormally high concentrations of lipids (fats) in the blood stream ^[1]. Hyperlipidaemia is caused by excess lipids in the diet or by abnormal lipid and lipoprotein metabolism ^[2] in the body. Hyperlipidaemia is a major health problem in Nigeria and other developing countries ^[3]. It evokes damages in various tissues, which in turn deregulate the cellular functions ^[4]. Hyperlipidaemia can cause atherosclerosis which occurs when cholesterol is deposited on the walls of the blood vessels ^[5]. Narrowing of the walls of the blood vessels reduces the flow of blood and if not treated may lead to complete blockage of the blood vessels. Atherosclerosis is the precursor of major cardiovascular diseases ^[6].

Prolonged hyperlipidaemia can also lead to non alcoholic fatty liver disease - a situation whereby cholesterol accumulates in the liver causing congestion ^[7]. Hyperlipidaemia also leads to oxidative stress in the body, causing reduction of antioxidant enzymes activities in order to scavenge the free radicals formed during oxidative stress. Oxidation of LDL particles (lipid peroxidation) may also result due to formation of free radicals ^[8]. The by-products of lipid peroxidation perturb structural organisation and functions of the cell membrane, consequently leading to cell destruction ^[9] and hence leakage of enzymes into the serum.

Treatment of hyperlipidaemia involves non pharmacological options which include diet control ^[10], exercise and the pharmacological options which include the use of lipid-lowering drugs like statins ^[11]. Statins are a class of drugs used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase, which plays a central role in the production of cholesterol in the

liver. This enzyme catalyzes the conversion of HMG-CoA to mevalonate, an early and rate-limiting step in cholesterol biosynthesis ^[2].

Regular intake of fruits and vegetables have been said to be protective against cardiovascular diseases ^[12]. Fruits and vegetables are rich in fibre, antioxidants, vitamins and minerals ^[13]. Cabbage (*Brassica oleracea*) is a vegetable that belongs to the *Cruciferae* family. Cabbage is a rich source of nutrients such as minerals (Ca, K, P, Fe, Mg & Zn), vitamins such as B-complex vitamins and ascorbic acid, carbohydrates, fats, proteins, water and secondary metabolites such as indoles and sulforaphanes ^[14]. Cabbage is a good source of dietary fibre ^[14, 15] which forms a tight bond with bile in the intestine, binding up all the harmful toxins, cholesterol and the fat that it contains. Since the soluble fibre cannot be absorbed by the intestinal wall, neither can the bile that is attached to it, this fibre-bound bile ultimately leaves the body in a bowel movement, with its load of toxins, cholesterol and fat in tow ^[16]. This research was carried out to study the inclusion level of cabbage that may reverse or tend to ameliorate high-fat diet induced hyperlipidaemia.

Methods

Animals and Diets

Twenty four (24) female weanling albino rats with an average weight of 68.3 ± 4.7 g were obtained from the Animal House of the Department of Biochemistry, University of Ilorin, Nigeria. They were housed in wooden cages under standard conditions (25-29 °C, natural day and night cycles of approximately 12 hour each). The animals were randomly distributed into six groups with four animals in a group. The animals were acclimatised for one week before the beginning of the experiment. They were grouped and fed with different dietary formulations as shown in Table 1 and given water *ad libitum*. Group 1 served as the control group and was fed with control diet (NC). Group 2 as the hyperlipidemic group (HFD), was fed with high-fat diet for eight weeks. Group 3 was the reference drug-treated group (RFD) and was fed with high fat diet for eight weeks then administered with 10mg/kg of atorvastatin for the last four weeks. Group 4 served as Test group 1 (10% CBD); it was fed with high fat diet for a period of four weeks then the feed was changed to 10% cabbage based diet for the last four weeks. Group 5 served as test group 2 (25% CBD), and was fed with high fat diet for a period of four weeks then the feed was changed to 25%

cabbage based diet for the last four weeks. Group 6 served as test group 2 (50% CBD), was fed with high fat diet for a period of four weeks and then the feed was changed to 50% cabbage based diet for the last four weeks.

Table 1: Composition of formulated high fat and cabbage based diets

Ingredients g/kg	Control Diet (NC)	High-Fat Diet (HFD)	10% Cabbage-Based Diet (CBD)	25% Cabbage-Based Diet (CBD)	50% Cabbage-Based Diet (CBD)
Corn starch	512	212	412	262	12
Maize husk	40	40	40	40	40
Soybean	250	250	250	250	250
Sucrose	100	100	100	100	100
^a Soy bean oil	40	40	40	40	40
^b Vitamin/Mineral mix	50	50	50	50	50
D-Methionine	4	4	4	4	4
L- Lysine	4	4	4	4	4
Animal fat	-	300	-	-	-
Cabbage	-	-	100	250	500

^aSoy bean oil: Poly unsaturated fatty acids (58%), monounsaturated fatty acids (29%), saturated fatty acids (13%).

^bVitamin/Mineral mix: Vitamin A, 97650IU; Vitamin D2, 23715IU; Vitamin E, 69.75IU; Vitamin K, 13.95mg; Vitamin B2, 41.85mg; Vitamin C, 13.95mg; Niacin, 139.5mg; Pantothenic Acid, 41.85mg; Vitamin B6, 41.85mg; Vitamin B12, 0.1395mg; Folic Acid, 6.975mg; Biotin, 5.58mg; Choline Chloride, 1813.5mg; Cobalt, 1.395mg; Copper, 13.95mg; Iodine, 139.5mg; Inositol, 17.4375mg; Iron, 209.25mg; Manganase, 976.5mg; Selenium, 1.395mg; Zinc, 279mg.

Preparation of diets

Goat fat was used as the source of fat in the high fat diet. Cabbage was obtained, rinsed thoroughly with clean water, chopped and then oven-dried at 40°C to a constant weight. The dried cabbage was then pulverised using electric blender. Control diet was prepared using slight modification of the method described by Monike et al. (2011) ^[17]. The composition of the corn starch was reduced by 300 g and 300 g/kg of animal fat was added to make 30% the High-fat diet while the Cabbage-based diet(CBD) were also formulated by adding 10, 25 and 50 g/kg of the cabbage in place of corn starch. The components of the diet were thoroughly mixed and made into pellets to ensure good handling by the animals.

Assay kits and reagents

The assay kits used in determination serum lipids were products of AGAPPE Diagnostics, Switzerland. The assay kits used to determine AST and ALT were products of Randox Laboratories Limited, 55 Diamond Road, Crumlin, Country Antrim, BT29 4QY, United Kingdom. All reagents used were of analytical grade.

Biochemical analysis

The proximate analyses for control diet, cabbage based diets (10%, 25% and 50%) and high fat diet were determined according to the methods of AOAC, (2002) ^[18].

After eight weeks, the animals were sacrificed by jugular puncturing under anaesthesia using diethyl ether; blood was collected inside centrifuge tubes and centrifuged at 3000rpm for 20min. The clear serum was carefully decanted into plain specimen bottles and kept frozen until needed for analysis. High density lipoprotein cholesterol (HDL-c) was determined by the methods of Williams (1979) ^[19] and Gordon *et al* (1977)^[20] as modified by Rafai and Warnick (1994)^[21]. The low density lipoprotein cholesterol (LDL-c) was determined using the method of Crouse (1985) ^[22]. The methods of Arntz (1979) ^[23] and Flegg (1973) ^[24] were employed in determining the total cholesterol while triglycerides concentration was determined using the methods of Jacobs and VanDemark (1960) ^[25] as modified by Schettler and Nussel (1975) ^[26]. Cardiovascular disease risk was calculated as described by Fulks *et al.* (2009) ^[27] and Atherogenic Index (AI) was calculated as described by Solanki and Bhatt (2010) ^[28]. The determination of serum CK was based on the principle described by Rosalki (1967) [29] and Tietz (1994) ^[30]. The procedure described by Reitman and Frankel (1957) ^[31] was used for assaying the Activity of AST and ALT. The activity of SOD was determined using the method described by Mistrá and Fredoxich (1972) ^[32] while the concentration of malondialdehyde (MDA) was quantified according to the method of Nelson (2004) ^[33].

Statistical analysis

Data from all the various determinations were collected, statistically analysed and expressed as the mean $\pm$ SEM (n=4), for each group of rats using one-way analysis of variance (ANOVA) as determined by the use of SPSS version 22.

Results

Table 2: Proximate composition of high-fat and cabbage-based diets

Proximate Composition (%)	NC		HFD		10% CBD		25% CBD		50% CBD
Moisture content	7.42	±	4.60	±	7.93 ± 0.26 ^e		4.24 ± 0.08 ^b		5.88 ± 0.06 ^c
	0.14 ^d		0.12 ^a						
Dry matter	92.58	±	95.40	±	92.07	±	95.86 ± 4.39 ^a		94.12 ± 1.41 ^a
	6.29 ^a		5.8 ^a		4.13 ^a				
Crude protein	19.95	±	20.74	±	20.73	±	20.44 ± 0.46 ^{ab}		21.35 ± 0.48 ^b
	0.45 ^a		0.54 ^{ab}		0.50 ^{ab}				
Crude lipid	3.76	±	38.83	±	4.48 ± 0.08 ^b		4.97 ± 0.21 ^c		5.79 ± 0.26 ^d
	0.12 ^a		4.59 ^e						
Crude fibre	4.44	±	3.58	±	9.59 ± 0.39 ^c		15.70 ± 0.36 ^d		31.14 ± 0.31 ^e
	0.29 ^b		0.33 ^a						
Total ash	8.42	±	6.37	±	10.19	±	10.57 ± 0.31 ^c		11.09 ± 0.14 ^d
	1.07 ^b		0.12 ^a		0.10 ^c				
Total carbohydrate	56.01	±	25.88	±	47.08	±	44.18 ± 3.23 ^c		24.75 ± 0.22 ^a
	4.36 ^d		0.28 ^b		3.06 ^c				

Values with different (a-e) superscripts along the same column are significantly different ($P < 0.05$), n=4 replicates mean ± SEM.

NC, Control; HFD, High-fat diet group; RFD, Reference drug group; 10% CBD, 10% Cabbage-based diet; 25% CBD, 25% Cabbage based diet; 50% CBD, 50% Cabbage based diet.

Table 2 shows the proximate composition of the high-fat and the cabbage-based diets. From the table, it could be observed that the crude fat content of high-fat diet was significantly higher ($p < 0.05$) than the control and was significantly higher than other groups. The crude fat composition of cabbage-based diets were significantly higher than the control and significantly higher ($p < 0.05$) than each other and the difference was percentage-related.

Table 3: Serum Lipid Profile and Hepatic Lipids of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets

Groups	Serum Lipid Profile (mmol /l)				Liver Lipids (mmol/l)	
	TC	HDL	LDL	Triglyceride	TC	Triglyceride
NC	3.15 ± 0.52 ^a	2.56 ± 0.27 ^{bc}	1.35 ± 0.18 ^{ab}	2.03 ± 0.52 ^a	4.00 ± 0.63 ^a	2.79 ± 0.11 ^b
HFD	7.08 ± 0.33 ^d	1.44 ± 0.24 ^a	3.39 ± 0.21 ^c	3.12 ± 0.33 ^c	5.80 ± 0.05 ^c	3.60 ± 0.08 ^c
RFD	4.17 ± 0.13 ^b	3.41 ± 0.60 ^c	1.48 ± 0.13 ^{ab}	2.06 ± 0.13 ^a	4.39 ± 0.24 ^b	2.50 ± 0.06 ^a
10% CBD	5.39 ± 0.40 ^c	1.64 ± 0.28 ^a	1.58 ± 0.11 ^b	2.67 ± 0.40 ^{bc}	3.74 ± 0.59 ^a	2.40 ± 0.58 ^{ab}
25% CBD	5.43 ± 0.31 ^c	2.13 ± 0.53 ^{ab}	1.45 ± 0.08 ^{ab}	2.52 ± 0.31 ^{ab}	3.66 ± 0.93 ^a	2.48 ± 0.14 ^a
50% CBD	5.48 ± 0.09 ^c	2.83 ± 0.45 ^{bc}	1.54 ± 0.08 ^b	2.66 ± 0.09 ^b	4.36 ± 0.37 ^{ab}	2.37 ± 0.04 ^{ab}

Values with different superscripts (a-d) along the same column are significantly different ($P < 0.05$), n=4 replicates mean ± SEM.

TC, Total Cholesterol; HDL, High density lipoprotein; LDL, Low density lipoprotein. NC, Control; HFD, High-fat diet group; RFD, Reference drug group; 10% CBD, 10% Cabbage-based diet; 25% CBD, 25% Cabbage-based diet; 50% CBD, 50% Cabbage-based diet.

Table 3 shows the serum lipid profile and hepatic lipids of animals fed on high-fat diet and treated with cabbage-based diets. Except for HDL which was significantly lower ($p < 0.05$), the serum and hepatic lipids of rats fed on high fat diet were significantly higher ($p < 0.05$) than the control and other groups. Except for total cholesterol, the serum and hepatic lipids of the reference drug group were not significantly different ($p < 0.05$) from the 25% cabbage-based diet group.

Table 4: Atherogenic Index and Cardiovascular Disease (CHD) Risk Ratio of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets

Groups	Atherogenic Index (AI) (mmol/l)	CHD Risk Ratio
NC	1.15 ± 0.26 ^a	1.34 ± 0.33 ^a
HFD	5.21 ± 0.67 ^d	5.52 ± 1.25 ^d
RFD	1.28 ± 0.20 ^a	1.26 ± 0.19 ^a
10% CBD	3.03 ± 0.30 ^c	3.46 ± 0.43 ^c
25% CBD	2.65 ± 0.54 ^b	3.01 ± 0.64 ^{bc}
50% CBD	2.05 ± 0.24 ^b	2.10 ± 0.34 ^b

Values with different superscripts (a-d) along the same column are significantly different ($P < 0.05$), $n=4$ replicates $\pm$ SEM.

Atherogenic Index, AI; Cardiovascular Disease Risk, CHD Risk. NC, Control; HFD, High-fat diet group; RFD, Reference drug group; 10% CBD, 10% Cabbage-based diet; 25% CBD, 25% Cabbage-based diet; 50% CBD, 50% Cabbage-based diet.

Table 4 shows the atherogenic index (AI) and cardiovascular disease (CHD) risk ratio of animals fed on high-fat diet and treated with cabbage-based diets. From Table 4, it could be observed that the Coronary Heart Disease (CHD) risk ratio and the AI of animals fed on high fat diet were significantly higher ($p < 0.05$) than the control and other groups. The CHD risk ratio and AI of animals placed on reference drug were not significantly different ($p < 0.05$) from the control.

Table 5: Specific Enzyme Activity in the Liver, Heart and Serum of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets.

Groups	Specific Enzyme Activity (n mol min ⁻¹ mg protein ⁻¹)						
	ALT		AST			CK	
	Liver	Serum	Liver	Heart	Serum	Heart	Serum
NC	76.00 ± 6.45 ^b	2.73 ± 0.66 ^a	216.95 ± 6.45 ^b	239.26 ± 7.87 ^c	3.43 ± 0.30 ^a	71.86 ± 1.42 ^a	7.76 ± 1.26 ^a
HFD	62.07 ± 5.40 ^a	6.22 ± 1.11 ^{bc}	195.75 ± 6.40 ^a	168.86 ± 12.35 ^a	10.86 ± 0.59 ^d	158.37 ± 7.17 ^f	32.84 ± 0.05 ^f
RFD	69.88 ± 6.76 ^a	5.05 ± 0.53 ^b	236.56 ± 6.76 ^c	240.02 ± 28.48 ^{bc}	6.82 ± 0.29 ^c	94.88 ± 6.70 ^b	11.03 ± 0.94 ^b
10% CBD	74.74 ± 4.19 ^{ab}	3.27 ± 0.51 ^a	218.95 ± 12.19 ^b	202.65 ± 5.22 ^b	5.53 ± 0.19 ^b	138.17 ± 1.68 ^e	24.62 ± 1.36 ^c
25% CBD	77.12 ± 4.39 ^b	2.72 ± 0.86 ^a	221.49 ± 4.39 ^b	238.06 ± 2.39 ^c	3.75 ± 0.88 ^a	127.00 ± 3.11 ^d	15.20 ± 1.86 ^d
50% CBD	75.40 ± 3.12 ^{ab}	3.35 ± 0.73 ^a	240.08 ± 7.12 ^c	229.01 ± 12.91 ^c	3.34 ± 0.93 ^a	112.58 ± 0.12 ^c	12.70 ± 0.09 ^c

Values with different superscripts (a-f) along the same column are significantly different ($P < 0.05$), $n=4$ replicates mean $\pm$ SEM.

ALT (Alanine aminotransferase), AST (Aspartate transaminase), CK (Creatine kinase). NC, Control; HFD, High-fat diet group; RFD, Reference drug group; 10% CBD, 10% Cabbage-based diet; 25% CBD, 25% Cabbage-based diet; 50% CBD, 50% Cabbage-based diet.

Table 5 shows the specific enzyme activities of ALT, AST and CK in the liver, heart and serum of animals fed on high-fat diet and treated with cabbage-based diets. Except for the serum CK which was significantly higher ($p < 0.05$) than the control, the specific activities of all the enzymes in 25% CBD were not significantly different ($p < 0.05$) from the control. The specific activities of ALT, AST and CK were significantly higher in the serum of the untreated and reference drug treated groups and significantly lower ($p < 0.05$) in their organs when compared with the control.

Table 6: Concentration of Malondialdehyde (MDA) and Specific Activity of Superoxide Dismutase (SOD) in the Liver and Heart of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets

Groups	Conc. of MDA ($\times 10^{-6}$) (n mol ⁻¹ ml)		SOD Activity ($\times 10^3$) (n mol min ⁻¹ mg ⁻¹ protein)	
	Liver	Heart	Liver	Heart
NC	6.11 $\pm$ 0.48 ^{ab}	4.16 $\pm$ 0.09 ^b	12.11 $\pm$ 2.01 ^{cd}	4.16 $\pm$ 0.09 ^b
HFD	7.89 $\pm$ 0.29 ^c	5.56 $\pm$ 0.17 ^d	3.35 $\pm$ 0.66 ^a	5.56 $\pm$ 0.17 ^d
RFD	6.08 $\pm$ 0.91 ^{ab}	3.82 $\pm$ 0.24 ^b	2.79 $\pm$ 1.94 ^a	3.82 $\pm$ 0.24 ^b
10% CBD	5.28 $\pm$ 0.44 ^a	3.85 $\pm$ 0.38 ^{ab}	9.68 $\pm$ 0.20 ^c	3.85 $\pm$ 0.38 ^{ab}
25% CBD	6.29 $\pm$ 0.11 ^b	3.42 $\pm$ 0.07 ^a	9.25 $\pm$ 0.81 ^c	3.42 $\pm$ 0.07 ^a
50% CBD	5.50 $\pm$ 0.36 ^a	4.35 $\pm$ 0.16 ^{bc}	6.88 $\pm$ 0.14 ^b	4.35 $\pm$ 0.16 ^{bc}

Values with different superscripts (a-d) along the same column are significantly different ($P < 0.05$), n=4 replicates mean $\pm$ SEM.

MDA (Malondialdehyde), SOD (Superoxide Dismutase). NC, Control; HFD, High-fat diet group; RFD, Reference drug group; 10% CBD, 10% Cabbage-based diet; 25% CBD, 25% Cabbage-based diet; 50% CBD, 50% Cabbage-based diet

Table 6 shows the concentration of malondialdehyde (MDA) and specific activity of superoxide dismutase (SOD) in the liver and heart of animals fed on high-fat diet and treated with cabbage-based diets. While the concentration of MDA in the untreated group was significantly higher ($p < 0.05$) than the control, the activities of SOD were significantly lower ($p < 0.05$) than the control.

Discussion

Africans as typified by Nigerians, eat lots of fatty meats as pepparsoups and other delicacies which expose them to the risks associated with high fat diets. Intake of high amounts of saturated and unsaturated fatty acids have been implicated in the etiology of hyperlipidaemia [34,35, 10, 2] and could be said to be responsible for the induction of hyperlipidaemia in the rats [2]. High-fat diet prepared with animal fat was evidently rich in saturated and unsaturated fatty acids (Table 2). Dietary fibres have been implicated in reduction of blood lipids. Therefore the inclusion of cabbage-based diets at different levels was carried out to study the effectiveness of cabbage as a source of dietary fibre in curbing high fat diet-induced hyperlipidaemia.

The crude fibre in the cabbage-based diets were significantly higher ($p < 0.05$) than that of the control and this fibre content was related to the percentage cabbage content of the diets (Table 2). This is because cabbage is rich in dietary fibre. The crude fibre content of the high-fat diet was significantly lower than that of the control as determined by the feed formulation- rich in saturated and unsaturated fatty acids present in high-fat diet. The cabbage-based diets also contained significant amounts of lipids which might be due to unsaturated lipids of the goat fat and the fatty acids present in cabbage. Oil has been extracted from cabbage and this oil has been reported to be effective against the treatment of ulcer and cancer among other diseases in humans^[14]. Cabbage has also been reported to be rich in fat soluble vitamins such as vitamin E and vitamin K and these vitamins can be found in the oil present in cabbage^[14]. Also, from Table 2, it could be observed that the ash contents of cabbage based diets were significantly higher ($p < 0.05$) than the control and significantly different ($p < 0.05$) from each other. This significant difference was percentage related. Reports have shown that cabbage is a good source of vitamins (such as B-complex vitamins and ascorbic acids), minerals (such as Ca, K, P, Fe, Mg and Zn) and antioxidants^[14, 15, 36]. The vitamins and minerals serve as coenzymes and cofactors in various metabolic reactions in the body and thus aid the absorption and utilization of nutrients in the body. A high amount of total ash is usually an indication of high amount of inorganic mineral content^[38]. The total ash content of the cabbage-based diets were significantly higher ($p < 0.05$) than that of the control because of the presence of high amounts of minerals in cabbage as reported previously in literature^[14, 15, 36].

Intake of high-fat diet has been known to induce hyperlipidaemia in previous studies^[2, 10, 35].

The results of this study (Table 3) show that except for total cholesterol, 25% cabbage-based diet (CBD) treated group was able to compare favourably with the reference drug in the treatment of hyperlipidaemia. 10% CBD treated group was not able to efficiently reduce blood lipids but 25% CBD efficiently reduced hepatic and serum lipids. This might be as a result of the percentage of cabbage in the 25% CBD being much higher than the percentage of cabbage in the 10% CBD which might not have been sufficient enough to reduce blood and hepatic lipids. The poor performance of the 50% cabbage-based diet in comparison to the 25% might mean that the 50% is not the effective percentage supplementation required for

reduction of serum and hepatic lipids in experimental animals and probably in man. It might also be as a result of the antinutrients present in cabbage to counter the effects of the nutrients in the 50% CBD because of the high percentage of cabbage in the diet ^[13].

Coronary heart disease (CHD) risk as the name suggests is a parameter used to determine the risks of exposure of an individual to coronary heart disease (CHD) ^[50]. The CHD risk can be defined as the ratio of total cholesterol (TC) to high density lipoprotein (HDL-c) ^[46, 47]. Just like myocardial infarction, CHD is also a cardiovascular disease. The reference drug used in this study was able to reduce the CHD risk to normal while the 10%, 25% and 50% CBD were able to reduce the CHD risk in a percentage-dependent manner on cabbage. These reductions were however not fully compared with the control and the reference drug treated groups.

Atherogenic index is a direct pointer to exposure to atherosclerosis which is a precursor of all cardiovascular diseases. High atherogenic index may suggest or imply that atherosclerotic plaques have been deposited on the walls of the arteries ^[39, 40]. These plaques are caused primarily by deposition of low density lipoprotein (LDL) on the walls of the arteries and may lead to partial or complete blockage to the flow of blood in the arteries. This situation exposes the individual to all forms of cardiovascular diseases (CVD) especially myocardial infarction in the case of complete blockage of the arteries ^[2]. The result of this study suggests that although the cabbage based diet was effective in the reduction of atherogenic index, it was not as effective as the reference drug (atorvastatin). The long term effects of treatment with a cabbage based diet might however give a better result.

Reduction of the activities of ALT and AST in the liver of the untreated (HFD) and ALT in the reference drug treated group (RFD) with corresponding increase in the activities of these enzymes in the serum (Table 5) may be as a result of damage to the membranes *in the organs*. Elevation of hepatic aspartate transaminase activity (AST) in the 50% CBD and reference drug treated groups suggests localised system toxicity of the reference drug and the high percentage of cabbage in the diet. This also suggests that there was increased synthesis of aspartate transaminase (AST) in the liver to overcome the damage which then became excess as observed in the results of this study. Increase in the activity of serum creatine kinase (CK) has been reported to be an indication of predisposition to muscle

damage, brain damage and myocardial infarction ^[34, 41]. The results in Table 6 suggest that the hyperlipidemic rats might have been exposed to oxidative stress. This is seen in the reduction of superoxide dismutase (SOD) activity in the liver and hearts of the untreated hyperlipidemic group and also the liver of the reference drug treated group. These findings also correspond to the increase in malondialdehyde (MDA) concentration in the heart and liver of the untreated group. High concentration of malondialdehyde is a marker of lipid peroxidation in tissues ^[42, 43]. Since membranes are mainly made up of lipids, it is therefore in order to conclude that there was a disruption in the integrity of the membranes of the heart of the untreated group. This disruption in membrane integrity is suggested to have lead to the leakage of heart and liver enzymes into the serum, thus increasing the serum specific activities of ALT, AST and CK as compared to the control.

In the CBD- treated groups, there was no significant difference ($p>0.05$) in the activities of the antioxidant enzymes (SOD and catalase) and the concentration of lipid peroxidation marker (malondaldehyde) when compared to the control. This result was anticipated since the serum and hepatic activities of AST and ALT were not significantly different from the control in the CBD-treated groups. This simply implies that cabbage was able to partially restore oxidation of membrane lipids, protect the integrity of the membranes and thus prevented leakage of enzymes from the organs into the serum. From the results, it could be seen that leakage of aspartate transaminase (AST) into the serum of reference drug treated group was from the liver and not from the heart but the leakage observed in high fat diet (Untreated group) was from the heart and liver. This was because the reference drug was protective only against heart diseases but appeared to pose inflicting damage to the hepatic tissues as reported by earlier studies ^[44, 45]. This result also suggests damage to the integrity of both the heart and liver of the untreated group. The leakage of aspartate transaminase (AST) enzymes into the serum of 10% cabbage-based diet treated group was from the heart only. This might be as a result of low percentage of cabbage (10%) in the diet.

Conclusion

The results of this study showed that high-fat diet formulated with goat fat was able to induce hyperlipidaemia, elevate heart disease parameters and cause damage to membrane lipids of the heart and liver. Cabbage-based diet of different percentages were however, able to significantly reduce ($p < 0.05$)

blood lipids but not to normal. Cabbage-based diet (25%) was however as effective as the reference drug and more preferable to the reference drug because the reference drug was protective only against heart diseases but posed potential damage to the hepatic tissues because of leakages of enzymes from the liver into the serum as a result of damage caused to the membrane lipids of the liver.

List of abbreviations used:

TC, Total Cholesterol;

HDL, High density lipoprotein;

LDL, Low density lipoprotein

NC, Control

HFD, High-fat diet group

RFD, Reference drug group

CBD, Cabbage-based diet

AST, Aspartate transaminase

ALT, Alanine transaminase

SOD, Superoxide dismutase

LDL-c, LDL-cholesterol

MDA, Malondialdehyde

Competing interests: None

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Authors' information:

Professor H. O. B. Oloyede is a former and the pioneer Vice-Chancellor of Fountain University, Osogbo , Osun State, Nigeria and a Professor of Biochemistry in the University of Ilorin, Ilorin, Nigeria.

Professor A. T. Oladiji is the Director, Centre for Research Development and In-House Training (CREDIT), and a Professor of Biochemistry, University of Ilorin, Ilorin, Nigeria.

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Table Legends:

Table 1: Composition of formulated high fat and cabbage based diets.

Table 2: Proximate composition of high-fat and cabbage-based diets

Table 3: Serum Lipid Profile and Hepatic Lipids of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets

Table 4: Atherogenic Index and Cardiovascular Disease (CHD) Risk Ratio of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets

Table 5: Specific Enzyme Activity in the Liver, Heart and Serum of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets

Table 6: Concentration of Malondialdehyde (MDA) and Specific Activity of Superoxide Dismutase (SOD) in the Liver and Heart of Animals Fed on High-Fat Diet and Treated with Cabbage-Based Diets