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Bigi Soft Drinks might Induce Hyperglycemia and Hyperlipidemia in Wistar Rats

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Authors' Contributions

This work was carried out in collaboration with all authors. Author AIA conceptualized and designed the study, and also wrote the manuscript. Author JAE managed the analyses of the study. Author EOO managed the literature searches. Author VNO wrote the protocol while Author UO performed the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Background: Bigi soft drinks are carbonated drinks produced by Rite Foods Limited. The company is an indigenous company in Nigeria. Before 2016, Coca-cola bottling company and 7up bottling company products were the dominant soft drinks in Nigeria. Rite Foods Limited introduced carbonated soft drinks into the Nigerian market in 2016 and have favourably competed with the existing products. As at today, Bigi soft drinks are the dominant soft drinks in Nigeria because of their palatable taste, large volume and low price.
Aim: This study sought to investigate the effect of Bigi soft drinks on fasting blood glucose and lipid profile of Wistar rats.
Methods: Thirty-five adult Wistar rats were used for this study. They were randomly divided into seven groups of five rats each after seven days acclimatization. They were treated accordingly: animals in group 1 were administered distilled water, those in group 2 were administered Bigi Cola,

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those in group 3 were administered Bigi Apple, those in group 4 were administered Bigi Tropical, those in group 5 were administered Bigi Orange, those in group 6 were administered Bigi Lemon and Lime, while those in group 7 were administered Bigi Chapman. The administration was done orally at a dose of 3 mL per 100 g body weight 12 hourly for fourteen days. At the end of the administration period, the animals were fasted overnight and anaesthetized using diethyl ether. Blood samples were collected by cardiac puncture. Fasting blood glucose and lipid profile were determined using standard methods.

Results: All the soft drinks used in this study (except Bigi Lemon and Lime) significantly increased the fasting blood glucose of animals. All the Bigi soft drinks (except Bigi Cola) significantly increased triglyceride, total cholesterol and VLDL of animals when compared with control at $p<0.05$ respectively. The soft drinks also perturbed the HDL and LDL of animals used in this study.

Conclusion: The result of this study implies that Bigi soft drinks might be deleterious to health as far as hyperglycemia and hyperlipidaemia is concern. This does not automatically translate to such effect on humans. However, individuals with a diabetic family history should minimize their consumption of these drinks.

Keywords: Bigi soft drinks; fasting blood glucose; lipid profile; diabetes; cardiovascular diseases.

1. INTRODUCTION

Carbonated soft drinks are sweetened water-based nonalcoholic beverages mostly with balance acidity [1]. They are also known as ready-to-drink beverages. Soft drinks are frequently flavoured and coloured and the principal component being water which is needed for hydration. Soft drinks are commonly consumed by both young and old people [2,3]. A notable finding of Wolff and Dangsinger [4] reported that weight gained was more dramatic from soft drinks when compared with fruit punches and fruit juice. Also, intake of fruit juice was not associated with an increased risk of type-2 diabetes. This could be because of the low glycemic index (GI) of fruit juice, soluble fibre, or other constituents of fruit juice that could be beneficial, as the authors suggested [5].

Bigi soft drinks are carbonated drinks produced by Rite Foods Limited. The company is an indigenous company in Nigeria. Before 2016, Coca-cola bottling company and 7up bottling company products were the dominant soft drinks in Nigeria. The Rite Foods Limited introduced carbonated soft drinks into the Nigerian market in 2016 and have favourably competed with the existing products. As at today, Bigi soft drinks are the dominant soft drinks in Nigeria because of their palatable taste, large volume and low price. They are produced into different products as shown in Fig. 1. These products include Bigi Soda, Bigi Cola, Bigi Bitter Lemon, Bigi Apple, Bigi Chapman, Bigi Tropical, Bigi Orange and Bigi Lemon and Lime.

The composition of each Bigi product as shown on their label is presented in Table 1.

Fig. 1. Bigi Carbonated Soft Drinks

Previous study revealed that a woman with high intake of sugar-sweetened soft drinks tends to be less physically active; also, she has high total calories and low protein, alcohol, magnesium and cereal fibre [4]. Also, intake of total carbohydrate, sucrose and fructose, as well as the overall glycemic index, was high in this woman. In essence, this woman has a dietary pattern and lifestyle that led to increased risk of several disease states, including obesity, type -2 diabetes and cardiovascular diseases [6].

Sugar-sweetened beverages consumption as a marker of an unhealthy lifestyle has the potential of being a quick screening test for the increase of obesity and type-2 diabetes, but it requires validation [7-10]. Because of the large number of calories in sugar-sweetened soft drinks and the relationship between the consumption of these drinks and weight gained, reducing sugar-sweetened beverage consumption may be the simple opportunity to curb the obesity epidemic [11,12]. Obesity is now a complex worldwide problem, resulting from a combination of genetic, behavioural, cultural and environmental influence that calls for not only behavioural changes at individual levels, but also changes in public

Table 1. Composition of Bigi soft drinks

	Bigi cola	Bigi apple	Bigi orange	Bigi lemon and lime	Bigi tropical	Bigi bitter lemon	Bigi chapman
Energy (Kcal)	48	50	49	51	49	55	54
Fats (g)	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5
Carbohydrate (g)	12	12	12	13	12	14	13
Fibre (g)	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5
Protein (g)	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5
Salt (g)	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01
Sodium (g)	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005	<0.005
NAFDAC registration number	08-3829	08-3830	08-3831	08-3832	08-3833	08-3834	08-8183

policy, social, environmental, and cultural norms [13,14].

The world health organization (WHO) and the food and agriculture organization submitted a report in April 2003 concluding that many deaths attributed to chronic diseases are due to obesity and outlined how millions of people around the world can avoid chronic diseases through diet and exercise [15]. In the 1960s, for example, diabetes mellitus was said to be rare in the African continent with a prevalent rate of 0.5% and the prevalent rate, then, in South Africa and North Africa is the highest, but in 1992, Nigeria has a prevalent rate of 2.8% as discovered by the Nigerian National Expert Committee on non-communicable diseases with more prevalence in Urban areas compared to rural areas [16]. This is as a result of gradual westernization, leading to an increase in the number of soft-drinks manufacturing companies. The traditional habit of giving water to a visitor is now replaced by soft drinks or alcohol, hence the need to assess their effects in raising the blood glucose concentration, and lipid profile being the major factors associated with diabetic mellitus and cardiovascular diseases. Diabetes mellitus is characterized by hyperglycemia together with the biochemical alteration of glucose and lipid peroxidation [17-19]. Lipid peroxidation, a free radical related process, is an uncontrolled, self-enhancing process disrupting membrane lipid and other cell components. Unlimited lipid peroxidation (LP) could be one of the main factors in the pathogenesis of diabetic complications [20,21]. This pathology is often related to the release of free radicals and caused oxidative stress [22]. During reoxygenation, hypoxanthine/ xanthine oxidase and arachidonic acid pathways are important sources of free oxygen radicals, which damage lipid membrane and lead to cytolysis and cell death [23].

The accumulation of lipid in diabetes is mediated through a variety of derangement in the metabolic and regulatory process especially insulin deficiency thereby rendering the diabetic patient more prone to hypercholesterolemia and hypertriglyceridemia [24]. One of the major pathogenesis of lipid metabolism, disturbances in diabetes, is the increasing mobilization of fatty acid from adipose tissue and secondary elevation of the free fatty acid level in blood [25]. Lipid abnormalities such as hypercholesterolemia, hypertriglyceridemia, hyperphospholipidemia and fatty acid distribution changes are common in diabetic patients [14]. Consumption of soft drinks in Nigeria is becoming high, and these soft drinks are reported to contained high calories which tend to increase the risk of obesity, type-2 diabetes and cardiovascular diseases [26]. Therefore, there is need to study the effects of these soft drinks through the assessment of these parameters as indices that point to predisposed to diabetes mellitus and cardiovascular diseases to reduce the risk of obesity, type-2 diabetes and cardiovascular diseases.

2. MATERIALS AND METHODS

2.1 Collection of Soft drinks

Bigi soft drinks (Bigi Cola, Bigi Apple, Bigi Tropical, Bigi Oange, Bigi Lemon and Lime, Bigi Chapman) used in this study were purchased from Final Solution Catering Service shop at Odo-Ona, along Apata Road, Ibadan, Nigeria and were kept at room temperature.

2.2 Experimental Design

Thirty-five (35) adult Wistar rats (*Rattus norvegicus*) with bodyweight between 120 and

150 g were used for this study. They were acclimatized for seven (7) days during which they were fed *ad libitum* with standard feed and drinking water and were housed in clean cages placed in well-ventilated housing conditions (under humid tropical conditions) throughout the experiment. All the animals received humane care according to the criteria outlined in the 'Guide for the Care and Use of Laboratory Animals' prepared by the National Academy of Science and published by the National Institute of Health. They were randomly divided into seven groups of five rats each and were treated according to animals in group 1 were administered distilled water, those in group 2 were administered Bigi Cola, those in group 3 were administered Bigi Apple, those in group 4 were administered Bigi Tropical, those in group 5 were administered Bigi Orange, those in group 6 were administered Bigi Lemon and Lime, while those in group 7 were administered Bigi Chapman. The administration was done orally at a dose of 3 mL per 100 g body weight 12 hourly for fourteen days. At the end of the administration period, the animals were fasted overnight and anaesthetized using diethyl ether. Blood samples were collected by cardiac puncture.

2.3 Determination of Fasting Blood Sugar

Fasting blood sugar was determined according to the methods described by Airaodion et al. [27]. After the acclimatization period, animals used in this study were allowed to fast for twelve (12) hours before the commencement of administration. The blood glucose level was taken by sterilizing the tails of the animals with 10% alcohol, and cutting the tails using scissors then allowing the blood to touch the test strip which was inserted into a calibrated glucose meter (One-touch Glucometer, Acon Laboratory INC. San Diego, USA). This gave direct reading after 5 seconds in mg/dL. The blood glucose level of the rats before the commencement of administration was measured to know the normal blood glucose of the rats in each group. At the end of the administration, all the rats in each group fasted overnight and their fasting blood sugar was determined using a glucose meter. This was done to check and observe the effect of soft drinks on blood glucose level when compared to their initial glucose level (before the administration).

2.4 Determination of Lipids

Lipids were extracted and determined according to previously described methods [28,29].

2.5 Statistical Analysis

Data were subjected to analysis of variance using Graph Pad Prism. Results were presented as Mean ± standard deviation. One way analysis of variance (ANOVA) was used for comparison of the means followed by Tukey's (HSD) multiple comparison tests. Differences between means were considered to be significant at $p<0.05$.

3. RESULTS

The results of the effect of Bigi soft drinks on fasting blood glucose and lipid profile of Wistar rats are presented in tables 2 and 3 respectively.

4. DISCUSSION

Diabetes is a complex metabolic disorder associated with developing insulin resistance, impaired insulin signaling and β-cell dysfunction, abnormal glucose and lipid metabolism, sub-clinical inflammation and increased oxidative stress. These metabolic disorders lead to long-term pathogenic conditions including micro- and macro-vascular complications, neuropathy,

Table 2. Effect of Bigi Soft Drinks on the Fasting Blood Glucose (FBG) of Animals after 14 days of Administration

Treatment	Pre-treatment (mg/dL)	Post-treatment (mg/dL)	Increase in FBG (mg/dL)
Control	58.82±4.32	60.07±3.94	1.25±0.02[a]
Bigi Cola	55.28±2.90	72.73±9.46	17.45±0.13[b]
Bigi Apple	61.25±3.28	74.96±4.30	13.71±1.11[c]
Bigi Tropical	54.93±5.35	77.83±5.74	22.90±1.08[d]
Bigi Orange	57.36±3.28	76.38±4.73	19.02±0.38[b]
Bigi Lemon and Lime	64.83±2.83	66.89±2.93	2.06±0.07[a]
Bigi Chapman	60.37±6.36	73.29±6.55	12.92±0.52[c]

Values are presented as Mean±S.E.M, where n = 5. Values with different superscript along the same column are significantly different at p<0.05

Table 3. Effect of Bigi soft drinks on the lipid profile of animals after 14 days of administration

Treatment	TC	TG	HDL	LDL	HDL:LDL	VLDL
Control	98.25±8.29^{a}	88.48±7.43^{a}	44.83±6.49^{a}	41.64±3.92^{a}	1.08±0.02^{a}	17.70±1.48^{a}
Bigi cola	101.63±5.34^{a}	91.93±8.47^{a}	40.87±3.74^{a}	47.92±4.73^{b}	0.85±0.03^{b}	18.39±1.70^{a}
Bigi apple	116.23±11.21^{b}	106.23±5.73^{b}	36.94±7.43^{b}	42.37±5.00^{a}	0.87±0.01^{b}	21.25±1.15^{b}
Bigi tropical	111.84±8.34^{c}	111.25±12.28^{c}	41.84±2.93^{a}	39.45±3.28^{a}	1.06±0.08^{a}	22.25±2.46^{b}
Bigi orange	118.28±6.43^{b}	109.39±3.86^{bc}	40.52±5.72^{a}	49.45±3.89^{b}	0.82±0.04^{b}	21.88±0.77^{b}
Bigi lemon and lime	124.43±12.21^{d}	121.28±9.83^{d}	32.67±3.92^{c}	56.74±4.32^{c}	0.58±0.02^{c}	24.26±1.97^{b}
Bigi chapman	115.63±9.22^{b}	110.00±7.83^{bc}	39.39±2.84^{b}	52.38±4.04^{bc}	0.75±0.03^{b}	22.00±1.57^{b}

Values are presented as Mean±S.E.M, where n = 5. Values with different superscript along the same row are significantly different at p<0.05
Legend: TC = Total Cholesterol, TG = Triglyceride, HDL = High Density Lipoprotein, LDL = Low Density Lipoprotein, VLDL = Very Low Density Lipoprotein

retinopathy, nephropathy, and a consequent decrease in quality of life and an increase in the rate of mortality [30]. Among the multiple risk factors underlining the incidence and progression of diabetes, diet is the main modifiable factor. Both experimental and epidemiological evidence has shown that consumption of vegetables rich in phenolic compounds and possess high antioxidant capacity may have an inverse relationship with the incidence and prevalence of diabetes [31]. Dietary control remains one of the most desirable avenues for the prevention and management of chronic degenerative diseases such as diabetes and cardiovascular diseases. This study sought to investigate the effect of oral intake of Bigi soft drinks in fasting blood glucose and lipid profile of Wistar rats.

In this study, all the Bigi soft drinks (except Bigi Lemon and Lime) were observed to significantly elevated the fasting blood glucose of animals at $p<0.05$ (table 2). This might be an indication that these drinks could predispose consumers to the risk of diabetes. One therapeutic approach for treating early stage of diabetes is to decrease postprandial hyperglycaemia. This is done by retarding the absorption of glucose through the inhibition of the carbohydrate-hydrolyzing enzymes, α-amylase and α-glucosidase, in the digestive tract. Consequently, activators of these enzymes determine an elevation in the rate of glucose absorption and consequently blunting the post-prandial plasma glucose rise [32,33]. Based on these findings, it could be suggested that these soft drinks may stimulate platelet aggregation and reduce vasodilatation, exerting an important role in the onset, development and progression of vascular complications caused by the hyperglycemic state [34]. However, Bigi Lemon and Lime had no significant effect on the fasting blood glucose of animals when compared with the control group after fourteen days of treatment. This might be that the flavor in it has the ability to suppress its sugar content. This is suggestive that of all the Bigi soft drinks used in this study, only Bigi Lemon and Lime is safe for diabetic patients and those predisposed to diabetes to consume.

Apart from the regulation of carbohydrate metabolism, insulin plays an important role in lipid metabolism. Insulin insufficiency, as in diabetes mellitus, is associated with hypercholesterolemia and hypertriglyceridemia, which have been reported to occur in experimental diabetic rats [35-37]. Hypercholesterolemia could result in a relative molecular ordering of the residual phospholipids, resulting in a decrease in membrane fluidity [38]. Accumulation of triglycerides is one of the leading risk factors in coronary heart disease (CHD). Lipid and lipoprotein abnormalities have been shown to play a major role in the pathogenesis and progression of several disease conditions [39].

In this study, total cholesterol and triglycerides concentrations were observed to increase significantly when animals treated with Bigi soft drinks (except for those treated with Bigi Cola) were compared with those of the control group at $p<0.05$ (Table 3). This could be that these soft drinks may increase the progression of CHD. Hypertriglyceridaemia has been reported in diabetic animals [40]. This was reported to be due to increased absorption and formation of triglycerides in the form of chylomicrons following exogenous consumption of a diet rich in fat or through increased endogenous production of triglyceride-enriched hepatic VLDL-cholesterol and decreased triglyceride uptake in peripheral tissues [40]. Hypercholesterolaemia has also been reported in diabetic animals [40]. This was attributed to the increased dietary cholesterol absorption from the small intestine following the intake of a high-fat diet in a diabetic condition [41]. Moreover, it can be conjectured that the lipid increasing effects of Bigi soft drinks could be due to the stimulation of hepatic cholesterol, triglyceride and possibly fatty acid synthesis [42]. The elevation in the triglyceride and total cholesterol observed in this study might be an indication that these soft drinks have the propensity to induce hypertriglyceridaemia and hypercholesterolaemia respectively making them be potent in the induction of diabetes mellitus and cardiovascular diseases. However, Bigi Cola showed no significant effect on the concentrations of triglyceride and total cholesterol of animals used in this study. This means that while other Bigi soft drinks used in this study may induce hypertriglyceridaemia and hypercholesterolaemia, Bigi Cola will not.

Hypertriglyceridaemia has also been reported to be a predictor of hypertension risk [43]. In the peripheral vascular system, endothelial cells rely on lipoproteins for the transfer of neutral sterols at this site. Although free cholesterol is transferred to HDL-cholesterol particles through the functioning of a designated HDL-cholesterol receptor, lecithin cholesterol acyltransferase (LCAT) serves to maintain the concentration toward the HDL core and preserve the

hydrophobic nature that facilitates the transfer. Esterification of cholesterol produces cholesterol ester (CE), which is concentrated in HDL core and may be transferred by cholesterol ester transfer protein (CETP) in the plasma compartment to apo-B containing lipoproteins in exchange for triglyceride. Increased CETP activity would suggest an enrichment of apo-B lipoproteins in plasma, while simultaneously decreasing HDL-cholesterol, and has generally been considered pro-atherogenic [44]. This probably explains why Bigi soft drinks may lead to an elevation in the risk of developing heart diseases since a low HDL-cholesterol/LDL-cholesterol ratio is deleterious and is indicative of a higher risk of cardiovascular diseases [45].

HDL-cholesterol and LDL-cholesterol are two of the four main groups of plasma lipoproteins that are involved in lipid metabolism and the exchange of cholesterol, cholesterol ester and triglycerides between tissues [46, 47]. Numerous population studies have shown an inverse correlation between plasma HDL-cholesterol levels and risk of cardiovascular disease, implying that factors associated with HDL-cholesterol protect against atherosclerosis. Some of these factors appear to have antioxidant and anti-inflammatory effects which may obviate processes that initiate atherogenesis [48,49].

Epidemiological studies have also shown that elevated concentrations of total cholesterol and/or LDL-cholesterol in the blood are powerful risk factors for coronary heart disease [50]. Most extra-hepatic tissues, although requiring cholesterol, have low activity of the cholesterol biosynthetic pathway. Their cholesterol requirements are supplied by LDL, which is internalized by receptor-mediated endocytosis. A major function of HDL-cholesterol is to enhance reverse cholesterol transport by scavenging excess cholesterol from peripheral tissues followed by esterification through lecithin: cholesterol acyltransferase and delivering it to the liver and steroidogenic organs for subsequent synthesis of bile acids and lipoproteins and eventual elimination from the body [51,52]. This role of HDL-cholesterol is responsible for its atheroprotective properties. HDL-cholesterol also regulates the exchange of proteins and lipids between various lipoproteins.

Also, HDL-cholesterol provides the protein components required to activate lipoprotein lipase which releases fatty acids that can be oxidized by the ß-oxidation pathway to release energy [46,47]. Most importantly, HDL-cholesterol can inhibit oxidation of LDL-cholesterol as well as the atherogenic effects of oxidized LDL-cholesterol by its antioxidant property [43]. LDL is a lipoprotein that transports cholesterol and triglyceride from the liver to peripheral tissues. It enables fat and cholesterol to move within the water-blood solution of the bloodstream. LDL is often called bad cholesterol; hence low levels are beneficial [53].

Unfortunately, the administration of some Bigi soft drinks (Bigi Apple, Bigi Chapman and Bigi Lemon and Lime) in this study caused a significant decrease in the serum level of HDL-cholesterol when compared with the control animals at $p<0.05$ (table 3). HDL-cholesterol is usually referred to as the 'good cholesterol' [28]. Again, administration of some Bigi soft drinks (Bigi Cola, Bigi Orange, Bigi Chapman, and Bigi Lemon and Lime) significantly increased the concentration of LDL-cholesterol (bad cholesterol) when compared with that of the control group at $p<0.05$. The combined effect of decreased HDL-cholesterol (good cholesterol) and increased LDL-cholesterol (bad cholesterol) in the present study resulted in a decreased HDL-cholesterol/LDL-cholesterol ratio in treated animals when compared with the control group. This strongly supports the notion that dietary supplementation with the extract of soft drinks may lead to an elevation in the risk of developing heart diseases because a low HDL-cholesterol/LDL-cholesterol ratio is deleterious and is indicative of a higher risk of CHD [54]. Although the activities of enzymes were not investigated in this study, it is possible that Bigi soft drinks increased the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase (the rate-limiting enzyme in cholesterol biosynthesis) [29]. This implies that the consumption of Bigi soft drinks are of adverse health importance as far as hyperlipidemia is a concern.

In this study, Bigi Lemon and Lime is of particular interest as it had no significant effect on the fasting blood glucose but adversely perturbed the lipid profile of animals when compared with the control animals after fourteen days of treatment. This implies that while it may not predispose one to diabetes, it might not be safe for people with cardiovascular diseases history and also cardiovascular disease patients to consume.

5. CONCLUSION

The result of this study implies that Bigi soft drinks might be deleterious to health as far as

hyperglycemia and hyperlipidaemia is concern. This does not automatically translate to such effect on humans. However, individuals with a diabetic family history should minimize their consumption of these drinks.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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