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JUICED *Telfairia Occidentalis* LEAF MODERATES SUGAR-INDUCED LIPIDS DISORDERS IN RATS

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ABSTRACT Dyslipidemia and other lipids dysregulation caused by high sucrose diet have been well documented. Modulation of lipids metabolic disorders have been approached with various therapeutics models of which plants components are reverberating. The comparative effect of the whole form, juiced, and pulp fractions of *Telfairia Occidentalis* leafy vegetable modified diets (TDs) on the sucrose-induced lipid dysfunction in the brain, heart and liver of the Wistar rats were investigated in this study. The Wistar rats were fed a diet of 30% energy supplied by sucrose (high sucrose diet) (SD) for twelve weeks. Three other rat groups were fed high sucrose diet modified with either the whole, juiced or pulp fractions to assess the effect of leafy vegetables as a food supplement. After twelve weeks, the selected lipids constituents were assayed, and the results were analysed statistically. This study showed that sucrose consumption within twelve weeks induced impaired lipids regulation in some selected organs by increasing ($p<0.05$) cholesterol in the heart and liver; triglycerides in the brain, heart and liver. Also, proportions of the organ to body weight (ORG: BDY) and lipids biomarkers were moderated by TDs in the three organs while SD decreased ($p<0.05$) ORG: BDY and increased ($p<0.05$) total lipids in the organs. Hence, the *T. Occidentalis*-modified diets reversed SD induced lipids toxicity across all the organs investigated. Additionally, the juiced fraction of the *T. Occidentalis*-modified diet showed to be more potent than other forms of *T. Occidentalis*-diet against sugar-induced lipids disorders.

Keywords: Atherogenic-Index, Juiced-vegetables, Lipid-disorders, Sucrose-diet, *T. Occidentalis*

INTRODUCTION

Technological advancement has made the human diet undoubtedly prescribed by taste while the dietary requirement for proper growth and healthy living is downplayed (Rippe & Angelopoulos, 2015). Sucrose, a common constituent of an energy-dense diet, is one of the major dietary components employed in various forms and amounts to meet the psychological desire has been shown to result in dietary assault and health complications (Jensen et al., 2018a). Its addition to foods, such as candies, soft drinks, and ice cream, has continued to cause *non-communicable pandemic disease* and sustained dramatic increase, occasioned by addiction (DiNicolantonio *et al.*, 2018). Consequently, a high sucrose diet remains one of the leading causes of global health burden, especially in developed societies (DiNicolantonio *et al.*, 2018).

Impaired lipids metabolism and regulation proceeds the pathogenesis of the non-alcoholic fatty liver disease (NAFLD), cardiovascular disease (CVD), and neurodegenerative disorders such as Alzheimer's disease (AD) (Bruce *et al.*, 2017). Sucrose-rich diet (SD) is implicated (Salau *et al.*, 2014) in these events, and impairment of the lipids homeostasis and metabolism vary from organ to organ (Ritze *et al.*, 2014).

The available management for sucrose induced metabolic assault like antilipidemic drugs, stress reduction, physical exercise, and dietary modification (Garcia *et al.*, 2019; Clement, 2020) appear promising but not without attending consequences and accompanied complications to health and lifestyle(Clement, 2020). As a result, there has been a spike in searching for more congenial and natural therapy such as fruits, cereal, and vegetables as a lasting remedy with most minor side-effects against sugar-induced lipids dysfunctions and disorders (Clement, 2020).

A significant percentage of the human diet are of plant origins like cereals, legumes, fruits and vegetables (Fuller *et al.*, 2016), which contain several bioactive compounds such as functional proteins (Montesano *et al.*, 2020), polyphenols, fibres. These bioactive compounds have been employed for multiple health benefits, including cancer management and prevention.

The tropical region of Sub-Sarahan Africa provides a habitat for a wide range of leafy vegetables; while some are seasonal, others are available in all seasons; among such leafy vegetables is *Telfairia Occidentalis* (Adeyeye & Omolayo, 2011). *T. Occidentalis* is a green leafy climbing plant widely cultivated in the Southern Nigerian region (Adeyeye & Omolayo, 2011). *T. Occidentalis* leaves are sparsely elucidated for phytochemistry purposes; however, their nutritional benefits are extensively documented (Adeyeye & Omolayo, 2011). Also, the organo-protective ability of this leafy vegetable has been reported (Nwanna & Oboh, 2007). Therefore, there is a shortage of information about the leafy vegetable as a food supplement against diet-induced lipid dysregulation, especially on target organs like the brain, liver and heart. Therefore, this study was set to investigate the comparative prophylactic potentials of the juiced and pulp fractions of *Telfairia Occidentalis* leaves by employing a more pleasant, dietary inclusion of this leafy vegetable into sucrose-calorie rich diets in rats.

MATERIALS AND METHODS

Experimental animals

Thirty Wistar rats, 4 – 6 weeks old, weighing 55g – 80g, were obtained from the Physiology department, Olabisi Onabanjo University, Ago-Iwoye, acclimatised for two weeks in a metabolic cage, fed with water and rat chow *ad-libtum*, with access to 12 hours light, daily.

Feed composition and preparation

Standard rat feeds were purchased from the Ladokun Feed, Ibadan, Oyo State, Nigeria.

Detail about the Feed composition is on the Supplementary document Page.

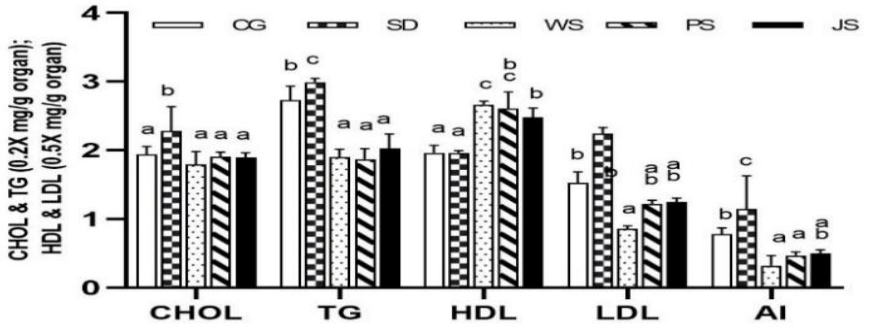
Animals grouping

After acclimatisation, the animals were randomly placed into five different groups of six members each.

Group I (CG):	100% Normal rat chow energy
Group II (SD):	30% Sucrose energy + 70% Normal rat chow e
Group III (WS):	15% Whole vegetable + 30% Sucrose energy +
Group IV (PS):	15% Pulp fraction (vegetable) + 30% Sucrose e
Group V (JS):	15% Juice fraction (vegetable) + 30% Sucrose e

Sample preparation

Animals were sacrificed through cervical dislocation, and organs (brain, liver and heart) were harvested, first rinsed in 1.15 % KCl solution, and kept in a sterile tube containing phosphate-buffer sucrose (7.2 pH). The buffer was prepared according to (Lam *et al.*, 1989).



Note: Bars of a parameter that have different letters are significant different at p<0.05

Figure 2: Heart Lipid profile of Rats fed *T. occidentalis* and High sucrose diet

Chemical reagents

All chemicals used for buffer preparation and extractions and lipids assays were of analytical grade, while Randox kits purchased from the UK were used for biomarkers of lipids profile.

Biochemical Analyses

Biomarkers of lipid profile, that is, cholesterol (CHOL), triglycerides (TG) and HDL-cholesterol (HDL), were assayed according to the procedure stated in the Randox, UK kits manuals using the methods of (Michaels *et al.*, 1958) (Hirano *et al.*, 2008), (Huang & Lin, 2012) respectively. The total lipids (LPD) were estimated according to the method of Folch with slight modifications. While LDL-cholesterol (LDL) atherogenic index (AI) was calculated according to (Friedewald *et al.*, 1972), (Abbott *et al.*, 1988), (Alladi & Radha Shanmugasundaram, 1989), respectively. Lipids estimation (The protocols for lipids assessment included in the supplementary document) while the somatogenic index was estimated.

The percentage ratio of the lipid profile biomarkers were calculated as follows:

Total Cholesterol/Total lipid (CHOL: LPD) = 100 X (Total cholesterol / Total lipids)

Triglycerides / Total lipid (TG: LPD) = 100 X (Triglycerides / Total lipids)

HDL-cholesterol / Total lipid (HDL: LPD) = 100 X (HDL / Total lipids)

Ethics approval

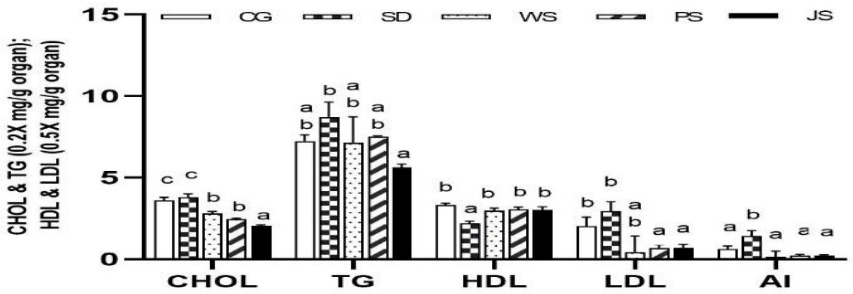
All procedures performed in studies involving animals were in accordance with the animal handling guidelines of the Redeemer's University Committee on Ethics for Scientific Research that governs the handling of laboratory animals. This article does not contain any studies with humans.

Statistical Analysis

The data were analysed; using descriptive statistics and analytical statistics (one-way ANOVA). The significance level was assessed using the Duncan Multiple Range Test at $p<0.05$, while values were expressed as the mean and standard error for six replicates (SPSS 23.0 software was used for data analysis).

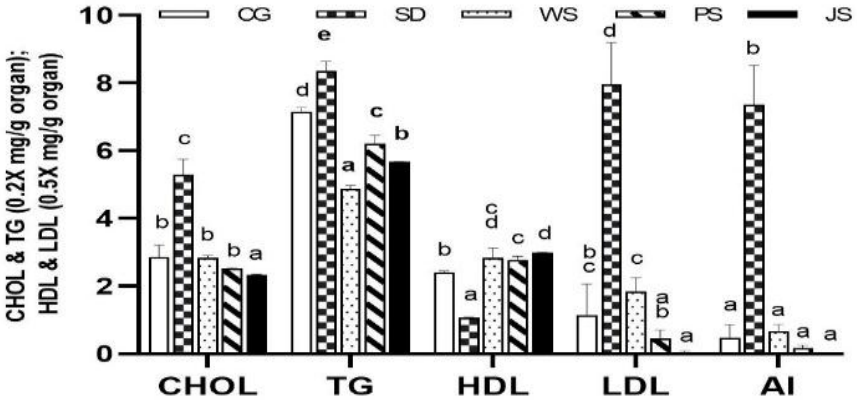
RESULTS

In this study, the comparative effect of two fractions (juice and pulp) and whole leaves of *T. Occidentalis* on lipid metabolism and homeostasis were evaluated in the brain, heart and liver of Wistar rats.



Note: Bars of a parameter that have different letters are significant different at $p<0.05$

Figure 1: Brain Lipid profile of Rats fed *T. occidentalis* and High sucrose diets



Note: Bars of a parameter that have different letters are significant different at p<0.05

Figure 3: Brain Lipid profile of Rats fed *T. occidentalis* and High sucrose diet

Table 1: Proportion of Brain Total Lipids to Lipids fractions of Rats fed *T. Occidentalis* and High Sucrose Diets

Group	BRN. (g)	BRN: BDY (%)	LPD (mg/g organ)	CHOL: LPD (%)	TG: LPD (%)	HDL: LPD. (%)
CG	1.94 ± 0.09^{b}	$0.83 \pm 0.06^{a,b}$	220.14 ± 25.14^{b}	8.2 ± 10^{c}	16.63 ± 2.8	3.06 ± 0.36^{c}
SD	1.68 ± 0.18^{a}	0.81 ± 0.09^{a}	296.41 ± 29.02^{c}	6.51 ± 1.34^{b}	15.14 ± 5.41	1.51 ± 0.32^{a}
WS	1.95 ± 0.1^{b}	0.9 ± 0.06^{b}	235.79 ± 27.72^{b}	$5.99 \pm 1.07^{a,b}$	14.88 ± 6.37	2.57 ± 0.48^{b}
PS	1.89 ± 0.02^{b}	$0.85 \pm 0.03^{a,b}$	249.43 ± 15.69^{b}	4.93 ± 0.30^{a}	15.15 ± 1.24	2.44 ± 0.25^{b}
JS	2.02 ± 0.03^{b}	$0.89 \pm 0.07^{a,b}$	190.49 ± 17.19^{a}	$5.43 \pm 0.55^{a,b}$	14.9 ± 1.88	3.17 ± 0.31^{c}

Values are expressed in mean ± standard deviation; Values in the same column but different superscripts are significantly different at p<0.05

Table 2: Proportion of Heart Total Lipids to Lipids fractions of Rats fed *T. Occidentalis* and High Sucrose Diets

Group	HRT. (g)	HRT: BDY. (%)	LPD. (mg/g organ)	CHOL: LPD (%)	TG: LPD. (%)	HDL: LPD. (%)
CG	0.97 ± 0.04^{c}	$0.41 \pm 0.02^{a,b}$	49.81 ± 3.02^{a}	19.52 ± 1.17^{b}	27.44 ± 2.17^{d}	7.92 ± 0.57^{c}
SD	$0.91 \pm 0.08^{b,c}$	0.44 ± 0.03^{b}	77.64 ± 2.65^{d}	14.69 ± 2.16^{a}	19.29 ± 0.68^{c}	5.07 ± 0.20^{a}
WS	0.82 ± 0.06^{a}	0.38 ± 0.03^{a}	60.6 ± 3.80^{b}	14.75 ± 0.72^{a}	15.71 ± 0.79^{b}	8.82 ± 0.41^{d}
PS	$0.88 \pm 0.03^{a,b}$	0.39 ± 0.02^{a}	71.48 ± 3.37^{c}	13.37 ± 0.76^{a}	13.13 ± 1.4^{a}	7.31 ± 0.65^{b}
JS	$0.87 \pm 0.04^{a,b}$	0.38 ± 0.04^{a}	68.59 ± 6.36^{c}	13.88 ± 0.80^{a}	14.81 ± 0.10^{b}	7.25 ± 0.29^{b}

Values are expressed in mean ± standard deviation; Values in the sample column but different superscripts are significantly different at $p<0.05$

Table 3: Proportion of Liver Total Lipids to Lipids fractions of Rats fed *T. Occidentalis* and High Sucrose Diets

Group	LVR. (g)	LVR: BDY. (%)	LPD. (mg/g organ)	CHOL: LPD (%)	TG: LPD. (%)	HDL: LPD. (%)
CG	7.64 ± 0.28^{b}	$3.25 \pm 0.16^{a,b}$	145.76 ± 9.18^{b}	9.83 ± 1.49^{b}	24.66 ± 1.96^{c}	3.32 ± 0.25^{c}
SD	8.67 ± 0.58^{c}	4.21 ± 0.29^{c}	219.95 ± 4.04^{e}	12.02 ± 1.11^{c}	19.01 ± 0.47^{b}	0.98 ± 0.02^{a}
WS	7.70 ± 0.49^{b}	3.57 ± 0.37^{b}	129.56 ± 6.15^{a}	11.00 ± 0.49^{c}	18.88 ± 1.01^{b}	4.39 ± 0.62^{d}
PS	6.80 ± 0.53^{a}	3.05 ± 0.33^{a}	189.86 ± 7.19^{d}	6.68 ± 0.22^{a}	16.35 ± 0.88^{a}	2.92 ± 0.10^{b}
JS	6.86 ± 0.53^{a}	3.00 ± 0.29^{a}	163.46 ± 4.00^{c}	7.16 ± 0.15^{a}	17.34 ± 0.42^{a}	3.65 ± 0.10^{c}

Values are expressed in mean ± standard deviation; Values in the same column but different superscripts are significantly different at $p<0.05$

DISCUSSION **Lipids biomarkers profile of the Brain of Rats**

The result from this present study showed that twelve weeks of SD consumption would increase the risk of neural-atherogenicity even when there were no significant ($p<0.05$) alterations in CHOL, TG and LDL levels; though, the HDL level depleted significantly (Fig. 1). Hottman et al. (2014) reported that HDL is crucial in lipids homeostasis regulation, especially for cholesterol cytosolic excretion. Also, Malgrange et al. (2015) observed that cholesterol homeostasis is tightly regulated in the brain. Excess secretion of these biomolecules is urgently exported across the blood-brain barrier (BBB) and transported to the liver. HDL level in the brain is independent of the brain cholesterol level because HDL in the brain is both endo and exogenous (Wang & Eckel, 2014). Therefore, the body attenuates the effect of sucrose on the brain lipids via the HDL production pathway, suggesting that HDL is crucial against sucrose-induced neuronal-lipids toxicity and consequent plaque formation, a substantial index of neurogenerative disorders.

It was observed that the *T. Occidentalis* diet showed neuroprotective potential against SD by increasing the brain HDL level significantly ($p<0.05$) and consequent significant ($p<0.05$) reduction in CHOL.

The JS group showed a significant decrease in TG level (Fig. 1); however, the AI level in WS and PS was also lowered significantly. This result agrees with Aworunse et al. (2018), who documented the therapeutic potential of *T. Occidentalis* on the animal brain.

The proportion of lipids biomarkers to total lipids in the brain of rats

This study (Table 1) revealed that consumption of SD for twelve weeks induced significant ($p<0.05$) neuronal weight gain. Also, SD-induced neuronal weight increase compliments the observed AI value (Fig. 1). The BRN: BDY was not altered despite the increased brain weight, though the brain weight (BRN) value tended towards atrophy. This observation concurs with (Murray & Chen, 2019), whose report revealed that SD consumption induced brain atrophy in Adolescence but in contrast with Zabetian-Targhi et al. (2019), who reported brain hypertrophy in aged human subjects fed high fructose diet.

T. Occidentalis-diet increases the neuronal HDL level as observed earlier (Fig 1) was further substantiated in Table 1 as there was a significant ($p<0.05$) reduction in brain LPD. Hence, it may account for the significantly elevated HDL: LPD, while the CHOL: LPD and TG: LPD. ($p>0.05$) were slightly altered. Temitope et al. (2018) reported that *T. Occidentalis* ameliorates neuronal toxicity. Thus, it may be suggestive that the neuroprotective effect of the *T. Occidentalis* diet may be due to its ability to stimulate HDL synthesis and influx to the neuronal cells, brain inclusive.

Lipids biomarkers profile of the Heart of Rats

The impact of SD consumption for twelve weeks resulted in significant ($p<0.05$) elevation of the cardiomyocytes CHOL, TG, LDL and AI levels in Wistar rats when compared with the CG (Fig. 2). Although the effect of SD was not significant ($p>0.05$) on the HDL level compared with the CG, the significantly high cardiomyocytes AI indicated that SD increases the risk of lipogenic-cardiomyopathy. This observation is in accord with Aboumsallem et al. (2019), who reported a diet containing high sucrose induced cardiomyopathy. In addition, Goldberg et al. (2012) stated that dietary sugar-induced toxic-lipids cardiomyopathy.

The heart derives over 80% of its energy from lipids, yet insulin action that is majorly stimulated by sugar intake is the predominant regulatory tool for cardiomyocytes' activities and cardio-lipogenesis (Goldberg *et al.*, 2018). Also, a recent study reported that an energy-dense diet like sucrose might indirectly upregulate the synthesis of free fatty acids (FFA) - a precursor of triglycerides

and cholesterol (Aboumsallem *et al.,* 2019). Hence, this suggests how the consumption SD within 12 weeks could trigger CHOL and TG accumulation in the heart and, as a result, increase the risk of atherogenicity by raising LDL level.

Consumption of *T. Occidentalis*-modified diet significantly ($p<0.05$) downregulated cholesterol, triglycerides and LDL in the heart of rats, with an increase in the HDL level, as well as a significant ($p<0.05$) decrease in the atherogenic risk factor (Fig. 2). Antioxidants are reported to stimulate HDL production and are a crucial complementary factor in lipids homeostasis regulation, and *T. Occidentalis* is one of the rich sources of antioxidant molecules. The antioxidant constituent of *T. Occidentalis* leafy vegetable may be one machinery that the diet explored to ameliorate the SD-induced cardio-atherogenic effect. The WS showed the highest anti-atherogenic potential.

The proportion of lipids biomarkers to total lipids in the heart of rats

Assessment of the ratio of lipids biomarkers (CHOL, TG and HDL) to the total lipids (LPD) in the heart revealed that cardial uptake of excess sugar from the diet provokes lipogenic imbalance by selectively increasing ($p<0.05$) the TG: LPD; consequently, increased the LPD significantly ($p<.0.05$) while, the CHOL: LPD, HDL: LPD were significantly ($p<.0.05$) lowered. Interestingly, this elevated TG: LPD did not translate to increased LPD: HRT and HRT: BDY values. The observed increase in TG: LPD recorded agrees with Goldberg et al. (2012). Also, this result indicated that the heart is resistant to short-term consumption of a high-sugar diet-induced toxic-lipids. Because cardiomyocyte mass was within the normal range (Table 2), this finding did not align with Mellor et al. (2010), who reported that the cardio-lipids homeostasis and metabolism are highly vulnerable to excessive sugar intake. One of the reasons for this discrepancy may be the slight variations in diet composition because a high-fructose diet was used as a model. According to Goldberg et al. (2012), increased glucose uptake promotes non-toxic lipogenesis processes; this suggests why the heart lipids fractions were relatively not altered except TG.

Furthermore, this study revealed that the CHOL: LPD SD group heart was significantly lower ($p<0.05$) than the CG group. According to Busserolles *et al.* (2002), short term sucrose consumption is beneficial to the heart; hence, complementing a plausible reason for the cardiomyocytes' non-hyperplasia-steatosis noted in the rats fed SD, despite the elevated cardiac steatosis. The decrease in the cholesterol level may be one of the complementary mechanisms that the heart utilises to mediate the exposure to sucrose-induced cardio-hypertrophy in the short-term period.

Clearly, the twelve weeks of SD consumption did not show notable lipids homeostasis deteriorating attribute in the heart. Nonetheless, *T. Occidentalis*-modified diet WS, PS andJS) further improve the cardiomyocytes lipids regulation by significantly ($p<0.05$) decreasing the cardio-steatosis risk indices, that is, the proportion of each lipid profile biomarkers assessed.

Also, amongst the three diets formulated, the JS seems to be more potent in enhancing the lipogenic integrity of the heart when compared with the PS and WS. Perhaps, the bioactive constituents of the juiced *T. Occidentalis* may be responsible for this modulating effect Salau et al. (2015) reported that juicing concentrates phytochemicals in leafy vegetables. Also, Oyeyemi et al. (2019) stated that juicing increased some phytochemicals in green vegetables. Hence, this may be one reason that the juice and whole forms of *T. Occidentalis*-modified diets improved the heart's lipid homeostasis in the study.

Lipids biomarkers profile of the Liver of Rats

The liver plays a unique role in modulating sugar metabolism by tightly sustaining physiological glucose concentrations in the circulatory system (Jensen *et al.,* 2018a). The consumption of SD for twelve weeks significantly ($p<0.05$) increased the levels of CHOL, TG, LDL and AI in the liver of the Wistar rats (Fig. 3). Liver metabolic disorders like NAFLD are induced by unregulated glucose uptake and gluconeogenesis in the hepatocytes (Lee *et al.,* 2017).

The elevated CHOL, TG, and LDL recorded in the liver of rats fed SD are indices of impaired lipids metabolism in the liver. This dysregulation cascaded into diminished HDL level and consequently increased the liver's LDL and AI. These findings agree with the works of (Sánchez-Lozada *et al.,* 2010), who reported that excess sugar consumption between 8 to 24 weeks might induce fatty liver. Also, Cydylo *et al.* (2017) showed that chronic fructose ingestion induced fatty liver disease in monkeys. One of the underlying mechanisms in which sucrose (glucose and fructose) induces liver steatosis is via indirectly suppression of lipolysis (beta-oxidation) and concurrently upregulating triglycerides synthesis (Jensen *et al.,* 2018b), caused by fructose molecules. According to Kantartzis *et al.* (2008), hepatic triglyceride synthesis would secondarily lead to low HDL and elevate LDL concentrations. It is considered a primary underlying mechanism for dyslipidemia and hepatic steatosis.

Studies have shown that one of the significant ways lipids induce hepatotoxicity and steatosis is the increment of reactive oxygen species (oxidative stress) through the upregulation of de-novo lipogenesis (Podszun *et al.,* 2020). However, plants' secondary metabolites (phytochemicals) and vitamins are known antioxidants (Nwanna & Oboh, 2007; Podszun *et al.,* 2020). Hence, this may account for one of the mechanisms in which *T. Occidentalis* modified diet moderates the metabolic imbalance of cholesterol, triglycerides, and HDL by significantly ($p<0.05$) reducing cholesterol and triglyceride levels while elevating hepatic HDL concentration (Fig. 3). Nwanna & Oboh (2007) reported that polyphenols present in *T. Occidentalis* and their ROS scavenging potential ameliorates hepatic injuries. Hence, revealing that *T. Occidentalis* may modulate hepatic HDL depletion by scavenging free radicals generated during the liver's lipogenic processes. Oh *et al.* (2015) documented that Licochalcone A is a flavonoid that inhibits lipogenesis in the primary hepatocytes selectively.

Fibres are the second considerable portion of vegetable pulp after water. They have been reported to repress sugar absorption in the intestine aggressively and consequently depress the postprandial glycemic index (Goff *et al.,* 2018). Also, (G. *et al.,* 2001) reported that dietary fibre could slow down intestinal activities. Hence, these fibre's potentials may be responsible for the significant increase ($p<0.05$) in hepatic HDL level recorded in the rats fed the whole and pulp fraction of the *T. Occidentalis* diet (Fig. 3).

The proportion of lipids biomarkers to total lipids in the liver of rats

Disruption in fat deposit and metabolic regulation is the hepatocellular hypertrophy index associated with sugar consumption (Mukonowenzou *et al.,* 2020). In this study, SD consumption significantly ($p<0.05$) elevated the LPD, CHOL: LPD and TG: LPD but decreased HDL: LPD ($p<0.05$). Consequently, it resulted in hepatic steatosis (increased LPD) and hypertrophy (elevated LVR: BDY) in Table 3 compared with the CG. These observations conform to, who reported that fructose overconsumption induces non-alcoholic fatty liver disease in rats.

The hepatocellular hypertrophy and non-alcoholic fatty liver indices induced by SD consumption were moderated in the groups fed *T. Occidentalis* diet (WS, PS and JS) by reducing the LVR, CHOL: LPD, TG: LPD and the hyperplasia index, that is, the LVR: BDY. This attenuating potential of *T.*

Occidentalis on NAFLD indices induced by SD consumption may be ascribed to the ensuing events of some bioactive molecules present in *T. Occidentalis* such as sterols, polyphenol and flavonoids, on triglycerides and cholesterols syntheses. Studies showed that plant quercetin selectively inhibits hepatocellular lipogenic pathways key enzymes (Donaldson *et al.*, 2019; Oh *et al.*, 2015; Wendel *et al.*, 2013). In addition, Kim *et al.*, (Kim *et al.*, 2016) documented the potential of polyphenols on glycemic regulation. Recent reports have also shown that dietary fibre consumption is associated with reduced NAFLD markers (Rietman *et al.*, 2018; Xia *et al.*, 2020), and *T. Occidentalis* is one of the rich sources(Okonwu *et al.*, 2018).

CONCLUSION

This work showed that diets with a 30% sucrose energy supply for twelve weeks have a higher risk to propagate lipid metabolic disorder and dysregulation events in the brain, heart and liver. This lipids dysregulation alters the triglycerides, cholesterol, HDL and LDL levels in the brain and liver (hepatic hyperplasia) but heart, where the HDL level was stabilised despite the elevated LDL level. While the *T. Occidentalis* modified diets (Juiced, Pulp, and Whole forms) ameliorated the dysfunctional lipid biomarkers in the three organs investigated. In addition, the juice fraction showed the highest potential in the brain and liver; the Whole form of leafy vegetable modified diet displayed the best lipid modulatory effect in the heart. Hence, diets rich in juiced *T. Occidentalis* may be a promising remedy against sugar diet-induced lipids disorders such as NAFLD and Alzheimer's Disease.

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Conflicts of interest

The authors of this study titled "Juiced *Telfairia Occidentalis* leaf Supplemented Diet Modulates Lipids Dysfunction In Rats Fed Sucrose Diet" declared no conflict of interest of any sort regarding this study.

REFERENCES

Abbott, R. D., Wilson, P. W., Kannel, W. B., & Castelli, W. P. (1988). High density lipoprotein cholesterol, total cholesterol screening, and myocardial infarction. The Framingham Study. *Arteriosclerosis: An Official Journal of the American Heart Association, Inc.*, *8*(3), 207–211. https://doi.org/10.1161/01.ATV.8.3.207

Aboumsallem, J. P., Muthuramu, I., Mishra, M., Kempen, H., & De Geest, B. (2019). Effective treatment of diabetic cardiomyopathy and heart failure with reconstituted HDL (Milano) in mice. *International Journal of Molecular Sciences*. https://doi.org/10.3390/ijms20061273

Adeyeye, E., & Omolayo, F. (2011). Chemical composition and functional properties of leaf protein concentrates of Amaranthus hybridus and Telfairia occidentalis. *Agriculture and Biology Journal of North America*. https://doi.org/10.5251/abjna.2011.2.3.499.511

Alladi, S., & Radha Shanmugasundaram, K. (1989). Induction of hypercholesterolemia by supplementing soy protein with acetate generating amino acids. *Nutrition Reports International*.

Aworunse, O. S., Bello, O. A., Popoola, J. O., & Obembe, O. O. (2018). Pharmacotherapeutic properties of Telfairia occidentalis Hook F.: A systematic review. In *Pharmacognosy*

Reviews. https://doi.org/10.4103/phrev.phrev_12_18

Bruce, K. D., Zsombok, A., & Eckel, R. H. (2017). Lipid processing in the brain: A key regulator of systemic metabolism. In *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2017.00060

Busserolles, J., Rock, E., Gueux, E., Mazur, A., Grolier, P., & Rayssiguier, Y. (2002). Short-term consumption of a high-sucrose diet has a pro-oxidant effect in rats. *British Journal of Nutrition*. https://doi.org/10.1079/bjn2002524

Clement W. Atlee. (2020). Overview of ideal antilipidemic drugs: Past, present and the future. *GSC Biological and Pharmaceutical Sciences*. https://doi.org/10.30574/gscbps.2020.11.3.0162

Cydylo, M. A., Davis, A. T., & Kavanagh, K. (2017). Fatty liver promotes fibrosis in monkeys consuming high fructose. *Obesity*. https://doi.org/10.1002/oby.21720

DiNicolantonio, J. J., O'Keefe, J. H., & Wilson, W. L. (2018). Sugar addiction: Is it real? A narrative review. In *British Journal of Sports Medicine*. https://doi.org/10.1136/bjsports-2017-097971

Donaldson, J., Ngema, M., Nkomozepi, P., & Erlwanger, K. (2019). Quercetin administration post-weaning attenuates high-fructose, high-cholesterol diet-induced hepatic steatosis in growing, female, Sprague Dawley rat pups. *Journal of the Science of Food and Agriculture*. https://doi.org/10.1002/jsfa.9984

Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*. https://doi.org/10.1093/clinchem/18.6.499

Fuller, S., Eleanor, B., Salman, H., & Tapsell, L. (2016). New Horizons for the Study of Dietary Fiber and Health : A Review American Association of Cereal Chemists. *Plant Foods for Human Nutrition*.

G., M., BSH, T., S., L., & PVG, M. (2001). Effect of dietary fiber on the activity of intestinal and fecal beta-glucuronidase activity during 1,2-dimethylhydrazine induced colon carcinogenesis. *Plant Foods for Human Nutrition*.

Garcia Ramirez, A. V., Filho, D. R., & Zotarelli Filho, I. J. (2019). Meta-analysis and Approach of the Real Impact of Anorexigenic Drugs in the Obesity in Humans: The Last Five Years of the Randomized Studies. *Current Diabetes Reviews*. https://doi.org/10.2174/1573399815666191113125247

Goff, H. D., Repin, N., Fabek, H., El Khoury, D., & Gidley, M. J. (2018). Dietary fibre for glycaemia control: Towards a mechanistic understanding. *Bioactive Carbohydrates and Dietary Fibre*, *14*, 39–53. https://doi.org/10.1016/j.bcdf.2017.07.005

Goldberg, I. J., Reue, K., Abumrad, N. A., Bickel, P. E., Cohen, S., Fisher, E. A., Galis, Z. S., Granneman, J. G., Lewandowski, E. D., Murphy, R., Olive, M., Schaffer, J. E., Schwartz-Longacre, L., Shulman, G. I., Walther, T. C., & Chen, J. (2018). Deciphering the role of lipid droplets in cardiovascular disease. In *Circulation*. https://doi.org/10.1161/CIRCULATIONAHA.118.033704

Goldberg, I. J., Trent, C. M., & Schulze, P. C. (2012). Lipid metabolism and toxicity in the heart. In *Cell Metabolism*. https://doi.org/10.1016/j.cmet.2012.04.006

Hirano, T., Nohtomi, K., Koba, S., Muroi, A., & Ito, Y. (2008). A simple and precise method for measuring HDL-cholesterol subfractions by a single precipitation followed by homogenous HDL-cholesterol assay. *Journal of Lipid Research*. https://doi.org/10.1194/jlr.D700027-JLR200

Hottman, D. A., Chernick, D., Cheng, S., Wang, Z., & Li, L. (2014). HDL and cognition in neurodegenerative disorders. In *Neurobiology of Disease*. https://doi.org/10.1016/j.nbd.2014.07.015

Huang, H. C., & Lin, J. K. (2012). Pu-erh tea, green tea, and black tea suppresses hyperlipidemia, hyperleptinemia and fatty acid synthase through activating AMPK in rats fed a high-fructose diet. *Food and Function*. https://doi.org/10.1039/c1fo10157a

Jensen, T., Abdelmalek, M. F., Sullivan, S., Nadeau, K. J., Green, M., Roncal, C., Nakagawa, T., Kuwabara, M., Sato, Y., Kang, D. H., Tolan, D. R., Sanchez-Lozada, L. G., Rosen, H. R., Lanaspa, M. A., Diehl, A. M., & Johnson, R. J. (2018a). Fructose and sugar: A major mediator of non-alcoholic fatty liver disease. In *Journal of Hepatology*. https://doi.org/10.1016/j.jhep.2018.01.019

Jensen, T., Abdelmalek, M. F., Sullivan, S., Nadeau, K. J., Green, M., Roncal, C., Nakagawa, T., Kuwabara, M., Sato, Y., Kang, D. H., Tolan, D. R., Sanchez-Lozada, L. G., Rosen, H. R., Lanaspa, M. A., Diehl, A. M., & Johnson, R. J. (2018b). Fructose and sugar: A major mediator of non-alcoholic fatty liver disease. In *Journal of Hepatology*. https://doi.org/10.1016/j.jhep.2018.01.019

Kantartzis, K., Häring, H.-U., & Stefan, N. (2008). Fatty liver and HDL-cholesterol: just a matter of quantity? *Future Lipidology*, *3*(3), 225–227. https://doi.org/10.2217/17460875.3.3.225

Kim, Y. A., Keogh, J. B., & Clifton, P. M. (2016). Polyphenols and glycémie control. In *Nutrients*. https://doi.org/10.3390/nu8010017

Lam, F. T., Mavor, A. I. D., Potts, D. J., & Giles, G. R. (1989). Improved 72-hour renal preservation with phosphate-buffered sucrose. *Transplantation*. https://doi.org/10.1097/00007890-198905000-00003

Lee, J., Kim, Y., Friso, S., & Choi, S. W. (2017). Epigenetics in non-alcoholic fatty liver disease. In *Molecular Aspects of Medicine*. https://doi.org/10.1016/j.mam.2016.11.008

Malgrange, B., Varela-Nieto, I., de Medina, P., & Paillasse, M. R. (2015). Targeting cholesterol homeostasis to fight hearing loss: A new perspective. In *Frontiers in Aging Neuroscience*. https://doi.org/10.3389/fnagi.2015.00003

Mellor, K. M., Ritchie, R. H., Davidoff, A. J., & Delbridge, L. M. D. (2010). Elevated dietary sugar and the heart: Experimental models and myocardial remodeling. In *Canadian Journal of Physiology and Pharmacology*. https://doi.org/10.1139/Y10-005

Michaels, G. D., Fukayama, G., Chin, H. P., & Wheeler, P. (1958). Technics for Separation of Plasma Cholesterol Esters for Determination of Iodine Value, and of

Cholesterol. *Proceedings of the Society for Experimental Biology and Medicine*. https://doi.org/10.3181/00379727-98-24197

Montesano, D., Gallo, M., Blasi, F., & Cossignani, L. (2020). Biopeptides from vegetable proteins: new scientific evidences. In *Current Opinion in Food Science*. https://doi.org/10.1016/j.cofs.2019.10.008

Mukonowenzou, N. C., Dangarembizi, R., Chivandi, E., Nkomozepi, P., & Erlwanger, K. H. (2020). Administration of ursolic acid to new-born pups prevents dietary fructose-induced non-alcoholic fatty liver disease in Sprague Dawley rats. *Journal of Developmental Origins of Health and Disease*. https://doi.org/10.1017/S2040174420000124

Murray, S., & Chen, E. Y. (2019). Examining Adolescence as a Sensitive Period for High-Fat, High-Sugar Diet Exposure: A Systematic Review of the Animal Literature. In *Frontiers in Neuroscience*. https://doi.org/10.3389/fnins.2019.01108

Nwanna, E. E., & Oboh, G. (2007). Antioxidant and hepatoprotective properties of polyphenol extracts from Telfairia occidentalis (Fluted Pumpkin) leaves on acetaminophen induced liver damage. *Pakistan Journal of Biological Sciences*. https://doi.org/10.3923/pjbs.2007.2682.2687

Oh, G. S., Lee, G. G., Yoon, J., Oh, W. K., & Kim, S. W. (2015). Selective inhibition of liver X receptor α-mediated lipogenesis in primary hepatocytes by licochalcone A. *Chinese Medicine (United Kingdom)*. https://doi.org/10.1186/s13020-015-0037-x

Okonwu, K., Akonye, L., & Mensah, S. (2018). Comparative Studies on Bioactive Components of Fluted Pumpkin, Telfairia occidentalis Hook F. Grown in Three Selected Solid Media. *Journal of Experimental Agriculture International*. https://doi.org/10.9734/jeai/2018/38334

Oyeyemi, A. W., Ugwuezumba, P. C., Daramola, O. O., & Onwelu, O. (2019). Comparative effects of *Zea mays* bran, *Telfairia occidentalis* and *Citrus sinensis* feeds on bowel transit rate, postprandial blood glucose and lipids profile in male wistar rats. *Nigerian Journal of Basic and Applied Sciences*. https://doi.org/10.4314/njbas.v26i1.9

Podszun, M. C., Alawad, A. S., Lingala, S., Morris, N., Huang, W. C. A., Yang, S., Schoenfeld, M., Rolt, A., Ouwerkerk, R., Valdez, K., Umarova, R., Ma, Y., Fatima, S. Z., Lin, D. D., Mahajan, L. S., Samala, N., Violet, P. C., Levine, M., Shamburek, R., … Rotman, Y. (2020). Vitamin E treatment in NAFLD patients demonstrates that oxidative stress drives steatosis through upregulation of de-novo lipogenesis. *Redox Biology*. https://doi.org/10.1016/j.redox.2020.101710

Rietman, A., Sluik, D., Feskens, E. J. M., Kok, F. J., & Mensink, M. (2018). Associations between dietary factors and markers of NAFLD in a general Dutch adult population. *European Journal of Clinical Nutrition*. https://doi.org/10.1038/ejcn.2017.148

Rippe, J. M., & Angelopoulos, T. J. (2015). Sugars and Health Controversies: What Does the Science Say? *Advances in Nutrition*, *6*(4), 493S-503S. https://doi.org/10.3945/an.114.007195

Ritze, Y., Bárdos, G., D'Haese, J. G., Ernst, B., Thurnheer, M., Schultes, B., & Bischoff, S. C. (2014). Effect of high sugar intake on glucose transporter and weight regulating hormones in mice and humans. *PLoS ONE*.

https://doi.org/10.1371/journal.pone.0101702

Salau, B. A., Ajani, E. O., Adebayo, O. L., And, A. A. K., & Osilesi, O. (2014). High sucrose diet modulates Calcium status in male albino rats: Possible implication on cardiovascular disease and dental caries. *Annals of Biological Sciences*.

Salau, B., Odufuwa, K., Adeosun, C., & Atunnise, A. (2015). Blanching and Juicing Effect on Flavonoids Contents in Commonly Consumed Leafy Vegetables in South West Nigeria. *International Journal of Biochemistry Research & Review*, *5*(3), 207–213. https://doi.org/10.9734/ijbcrr/2015/14230

Sánchez-Lozada, L. G., Mu, W., Roncal, C., Sautin, Y. Y., Abdelmalek, M., Reungjui, S., Le, M., Nakagawa, T., Lan, H. Y., Yu, X., & Johnson, R. J. (2010). Comparison of free fructose and glucose to sucrose in the ability to cause fatty liver. *European Journal of Nutrition*. https://doi.org/10.1007/s00394-009-0042-x

Temitope, A. O., Emmanuel, A. G., Akintola, A. O., Olabode, F. J., & Isaac, A. T. (2018). Free radical scavenging activity of Telfairia occidentalis extracts and their effects on iron-sulphate induced lipid per oxidation. *Pakistan Journal of Pharmaceutical Sciences*.

Wang, H., & Eckel, R. H. (2014). What are lipoproteins doing in the brainα. In *Trends in Endocrinology and Metabolism*. https://doi.org/10.1016/j.tem.2013.10.003

Wendel, A. A., Cooper, D. E., Ilkayeva, O. R., Muoio, D. M., & Coleman, R. A. (2013). Glycerol-3-phosphate Acyltransferase (GPAT)-1, but Not GPAT4, Incorporates Newly Synthesised Fatty Acids into Triacylglycerol and Diminishes Fatty Acid Oxidation. *Journal of Biological Chemistry*, *288*(38), 27299–27306. https://doi.org/10.1074/jbc.M113.485219

Xia, Y., Zhang, S., Zhang, Q., Liu, L., Meng, G., Wu, H., Bao, X., Gu, Y., Sun, S., Wang, X., Zhou, M., Jia, Q., Song, K., Wu, Q., Niu, K., & Zhao, Y. (2020). Insoluble dietary fibre intake is associated with lower prevalence of newly-diagnosed non-alcoholic fatty liver disease in Chinese men: A large population-based cross-sectional study. *Nutrition and Metabolism*. https://doi.org/10.1186/s12986-019-0420-1

Zabetian-Targhi, F., Srikanth, V. K., Smith, K. J., Oddy, W. H., Beare, R., Moran, C., Wang, W., & Callisaya, M. L. (2019). Dietary Patterns Are Not Associated with Brain Atrophy or Cerebral Small Vessel Disease in Older Adults with and without Type 2 Diabetes. *Journal of Nutrition*. https://doi.org/10.1093/jn/nxz139