Effects of Dietary Inclusions of Simple Sugars (Glucose, Fructose and Sucrose) on the Lipid Profile in the Spleen of Wistar Strain Albino Rats

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Abstract

Excessive consumption of dietary simple sugars is often associated with metabolic dysregulation of lipids and the progression of related disorders. Although hepatic and serum lipid alterations associated with high sugar intake have been widely studied, limited information exists regarding lipid accumulation in extrahepatic immune-associated tissues such as the spleen. The effects of dietary simple sugars, such as glucose, fructose, and sucrose, on the parameters of the splenic lipid profile in Wistar strain albino rats were examined in this research. One hundred healthy male Wistar rats (90–110 g) that were bought as a few-week-old neonates were divided into four main groups at random, which included control, glucose, fructose, and sucrose-treated groups. Each treatment group was further divided into three groups based on body weight: low (1 g/kg b.w.), medium (2 g/kg b.w.), and high-dose (4 g/kg b.w.). Sugars were constituted in distilled water and administered orally once daily every morning before food for ten weeks. Standard enzymatic assays were used to quantitatively measure splenic lipid parameters including total cholesterol (TC), triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C). Results showed that all sugar-treated groups' splenic TC, TAG, and LDL-C concentrations were considerably higher ($p < 0.05$) than those of the control group, whereas HDL-C levels were significantly lower. Fructose administration consistently produced the most pronounced alterations across all dosage categories. These findings demonstrate that chronic intake of dietary simple sugars can alter splenic lipid homeostasis, with fructose exhibiting the greatest dyslipidemic effect. The study suggests that excessive fructose consumption may contribute to metabolic disturbances involving altered lipid handling in peripheral tissues.

Keyword: Lipid Profile; Dietary Sugars; Obesity; Diabetes; Fasting Blood Sugar.

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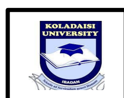
Introduction

Dietary sugars constitute a major component of modern nutrition and are extensively consumed in processed foods and beverages worldwide. Among these sugars, glucose, fructose, and sucrose are the most common simple carbohydrates incorporated into daily diets. While these sugars are vital for metabolic energy, excessive consumption has been progressively linked to metabolic disorders such as dyslipidemia, overweight, resistance to insulin, and diabetes mellitus (Bray et al., 2004). The increasing prevalence of these metabolic disorders has generated significant interest in understanding the biochemical and physiological consequences of excessive sugar consumption on different tissues and organs.

Lipid metabolism is essential for energy storage, membrane integrity, and cellular signaling. Disturbances in lipid homeostasis may result in associated derangements such as abnormal accumulation of cholesterol and triacylglycerol within tissues, thereby contributing to onset and progression of disorders of lipid metabolism (Nelson and Cox, 2021). Total cholesterol (TC), triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) are widely recognized biomarkers for evaluating alterations in lipid metabolism and cardiovascular risk (Grundy, 2016). High dietary sugar intake, especially fructose consumption, has been shown in earlier studies to increase dyslipidemia and aberrant lipid buildup (Stanhope et al., 2009). However, a disproportionate number of studies have focused primarily on serum and hepatic lipid alterations, with comparatively limited attention directed toward extrahepatic tissues such as the spleen.

The spleen is an important lymphoid organ involved in immune regulation, hematological balance, lipid recycling, and systemic inflammatory responses. Emerging evidence suggests that metabolic stress and altered lipid homeostasis may influence splenic physiology



through inflammatory and oxidative mechanisms (Hotamisligil, 2006). In addition, the spleen participates in lipoprotein clearance and immune-mediated regulation of lipid metabolism, making it a potentially relevant tissue in metabolic dysfunction (Ai et al., 2018). Despite these associations, information regarding the direct effects of dietary sugars on splenic lipid accumulation remains limited.

Fructose has garnered significant interest among dietary sugars due to its unique metabolic pathway and a tendency to facilitate lipogenesis more efficiently than glucose (Tappy and Lê, 2010). Sucrose, which contains both glucose and fructose moieties, may similarly contribute to alterations in tissue lipid metabolism. Understanding the tissue-specific effects of dietary sugars on splenic lipid homeostasis may therefore provide further insight into the systemic consequences of excessive sugar consumption.
By assessing splenic concentrations of TC, TAG, LDL-C, and HDL-C in Wistar strain albino rats, the current research focused on evaluating the effects of dietary intake of glucose, fructose, and sucrose on splenic lipid profile parameters.

Methodology

Experimental Animals and Ethical Approval

For this experiment, one hundred mature male Wistar albino rats in good condition with an initial body weight of 90–110 g were employed. The animals were obtained from the Department of Biochemistry's Animal House Facility at the Federal University of Agriculture in Abeokuta, Ogun State, Nigeria. They were housed in clean, well-ventilated plastic cages with a temperature of 25 ± 2°C, a relative humidity of 50–60%, and a 12-hour light/dark cycle. Before the experiment began, the rats were allowed to acclimate for two weeks. They also had unlimited access to clean drinking water and regular rat food. The Department of Biochemistry at Olabisi Onabanjo University, Ago-Iwoye's Institutional Research Ethics Committee approved all animal operations, which were carried out strictly in accordance with the rules for the use and care of laboratory animals (Reference: OOU/BCH/06/236).

Experimental Design and Sugar Administration

The animals were divided into four main groups at at random. These were control, glucose, fructose, and sucrose-treated groups. Low (1 g/kg), medium (2 g/kg), and high (4 g/kg) dose subgroups were created for each treatment group based on body weight (n = 10 per subgroup). Sugars were orally administered in 2 ml aliquots of distilled water using an orogastric cannula once daily for ten weeks. The control group received distilled water only for the period of the experiment.

Sample Collection and Extraction Protocol

The rats were humanely put to sleep under moderate anaesthesia at the conclusion of the ten-week treatment period. The spleen of each animal was carefully removed, wiped dry with filter paper, and weighed after being thoroughly cleaned of any leftover blood using ice-cold phosphate-buffered saline (PBS). A modified chloroform–methanol (2:1, v/v) approach based on Folch et al. (1957) and Bligh and Dyer (1959) was then used to extract tissue lipids.

In short, spleen samples were homogenised in an ice-cold chloroform-methanol combination using a glass-Teflon homogeniser. To enhance phase separation, the resultant homogenate was filtered and mixed with a 0.9% sodium chloride solution. After a 10-minute centrifugation at 3,000 rpm, the lower organic (lipid-containing) phase was carefully recovered and the top aqueous phase was discarded. The organic phase was then evaporated to dryness in a water bath at 40°C and partly suspended in chloroform before being stored at -20°C for further analysis.

Using commercially available enzymatic colorimetric assay kits, tissue triacylglycerol (TAG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) levels were measured in accordance with the manufacturer's instructions. These assays are based on enzymatic hydrolysis and oxidation reactions that yield a chromogenic product proportional to lipid concentration, which was measured spectrophotometrically. This combined extraction–enzymatic quantification approach is widely employed for accurate determination of lipid content in tissue homogenates (Rodríguez-Sureda and Peinado-Onsurbe, 2005).

Statistical Analysis

The mean ± standard error of the mean (SEM) is used to display the data. IBM SPSS Statistics version 28.0 was used for the statistical analysis. First, the Shapiro-Wilk test and Levene's test were used to confirm that the data distribution was normal and that the variances were homogeneous. After evaluating differences between experimental groups using one-way analysis of variance

(ANOVA), Tukey's post-hoc test was used for multiple comparisons. A probability value of $p < 0.05$ was considered statistically significant.

Results

Splenic lipid concentrations are affected by dietary simple sugars, as seen in Table 1.

Total Cholesterol (TC)

Splenic total cholesterol concentrations were significantly elevated in all sugar-treated groups compared with the control group ($p < 0.05$). The control group recorded the lowest TC value (130.57 ± 0.71 mg/dL), whereas progressive increases were observed with increasing doses of glucose, sucrose, and fructose. Among the glucose-treated groups, TC increased from 145.99 ± 1.72 mg/dL in the low-dose group to 161.08 ± 0.93 mg/dL in the high-dose group. Similarly, sucrose administration caused dose-dependent elevations, with the highest value observed in the SUC HIGH group (153.64 ± 0.93 mg/dL). Fructose treatment produced the greatest increase in TC concentration, particularly in the FRU HIGH group, which exhibited the highest TC level overall (164.59 ± 0.77 mg/dL).

Table 1: Effects of Different Sugar Treatments on Lipid Profiles in Rats Spleen

Group	TC (mg/dL)	TAG (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)
CONTROL	130.57 ± 0.71^{a}	131.50 ± 0.69^{a}	56.97 ± 0.95^{f}	47.29 ± 1.11^{a}
GLU LOW	145.99 ± 1.72^{c}	136.78 ± 0.48^{b}	44.48 ± 0.42^{d}	74.14 ± 1.55^{c}
GLU MED	153.62 ± 0.95^{d}	145.52 ± 0.37^{d}	36.31 ± 0.78^{c}	88.20 ± 1.25^{d}
GLU HIGH	161.08 ± 0.93^{e}	144.76 ± 0.49^{c}	24.19 ± 0.88^{a}	107.93 ± 1.69^{g}
SUC LOW	142.00 ± 0.94^{b}	130.88 ± 0.88^{a}	47.12 ± 0.52^{d}	68.70 ± 1.32^{b}
SUC MED	148.86 ± 0.48^{c}	134.64 ± 0.39^{b}	37.72 ± 0.73^{c}	84.26 ± 0.52^{d}
SUC HIGH	153.64 ± 0.93^{d}	142.79 ± 0.68^{c}	27.07 ± 0.51^{b}	98.01 ± 0.92^{f}
FRU LOW	144.26 ± 1.54^{b}	136.25 ± 0.41^{b}	47.21 ± 0.87^{e}	70.20 ± 1.01^{b}
FRU MED	158.67 ± 0.79^{e}	142.79 ± 0.68^{c}	36.68 ± 0.47^{c}	93.41 ± 0.57^{e}
FRU HIGH	164.59 ± 0.77^{f}	148.82 ± 0.45^{e}	24.75 ± 0.33^{a}	110.08 ± 0.50^{g}

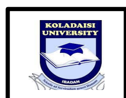
Note: With n = 10 animals per group, values are shown as mean ± standard error of the mean (SEM). Means with different superscript letters within the same column are significantly different ($p < 0.05$) as determined by one-way analysis of variance (ANOVA) followed by Tukey's post-hoc multiple comparison test. TC = total cholesterol; TAG = triacylglycerol; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; GLU = glucose; SUC = sucrose; FRU = fructose.

Triacylglycerol (TAG)

Splenic TAG concentrations were significantly altered following administration of dietary sugars ($p < 0.05$). The control group recorded a TAG level of 131.50 ± 0.69 mg/dL. While the SUC LOW group did not differ significantly from the control, medium and high - dose sugar administration generally resulted in significant TAG elevations. The GLU MED and FRU HIGH groups showed particularly elevated TAG levels of 145.52 ± 0.37 mg/dL and 148.82 ± 0.45 mg/dL, respectively. A progressive increase in TAG concentrations was evident across the sucrose and fructose - treated groups.

High-Density Lipoprotein Cholesterol (HDL-C)

HDL-C values were considerably lower in all sugar-treated groups compared to the control group ($p < 0.05$). The control animals exhibited the highest HDL-C level (56.97 ± 0.95 mg/dL), whereas substantial reductions were observed following glucose, sucrose, and fructose



administration. In the glucose-treated groups, HDL-C declined progressively from 44.48 ± 0.42 mg/dL in GLU LOW to 24.19 ± 0.88 mg/dL in GLU HIGH. Similar dose-dependent decreases were observed in sucrose- and fructose-treated animals. The lowest HDL-C values were recorded in the GLU HIGH and FRU HIGH groups.

Low-Density Lipoprotein Cholesterol (LDL-C)

In all sugar-treated groups, splenic LDL-C values were considerably higher than those in the control group ($p < 0.05$). The control group recorded the lowest LDL-C concentration (47.29 ± 1.11 mg/dL), whereas marked dose-dependent elevations were observed following glucose, sucrose, and fructose administration. LDL-C values increased from 74.14 ± 1.55 mg/dL in GLUC LOW to 107.93 ± 1.69 mg/dL in GLU HIGH. Fructose-treated animals exhibited the most pronounced increase, with the FRU HIGH group recording the highest LDL-C level overall (110.08 ± 0.50 mg/dL).

Discussion

The results of the study show that long-term use of dietary sugars including glucose, sucrose, and fructose causes severe dyslipidemia, which is characterized by decreased HDL-C, raised total cholesterol (TC), triacylglycerol (TAG), and low-density lipoprotein cholesterol (LDL-C). These changes were clearly dose-dependent, with the most noticeable effects seen at greater sugar consumption concentrations. Notably, fructose exerted the most severe impact on lipid homeostasis, followed by glucose and sucrose, suggesting differential metabolic handling and pathogenic potential among these sugars.

The observed increase in TC across all treatment groups is consistent with previous reports indicating that excessive simple sugar intake promotes hepatic cholesterol synthesis and accumulation (Stanhope, 2016). This effect may be mediated by activation of lipogenic transcription factors, such as sterol regulatory element-binding proteins (SREBPs), which encourage the liver to produce cholesterol (Shimano, 2001). The more noticeable increase seen in the fructose-treated groups confirms previous research showing that fructose evades important glycolysis regulatory stages, resulting in uncontrolled substrate flow through lipid synthesis pathways (Softic et al., 2016).

Similarly, the significant elevation in TAG levels observed in this study reflects enhanced hepatic de novo lipogenesis (DNL), a well-established consequence of high sugar consumption. Due to its preferred hepatic metabolism and capacity to boost the availability of acetyl-CoA, a form of precursor for the synthesis of fatty acids, fructose in particular has been demonstrated to quickly accelerate TAG synthesis (Hannou et al., 2018). A threshold effect, beyond which lipid metabolic pathways become dysregulated, is suggested by the non-significance in TAG level shown in the low-dose sucrose group.

The marked reduction in HDL-C across all sugar-treated groups is indicative of impaired lipid transport and altered cholesterol redistribution. Reduced HDL-C levels are commonly observed in metabolic diseases including atherosclerosis, which are typically linked to excessive sugar consumption and have been firmly linked to an increased risk of cardiovascular disorders (Taskinen et al., 2019).

The atherogenic danger of excessive sugar consumption is further highlighted by elevated LDL-C levels, especially in the high-dose fructose and glucose groups. According to Brown and Goldstein (2009), elevated LDL-C in this study may be directly related to increased hepatic production and/or decreased clearance of LDL particles. LDL-C is a major contributor to plaque formation and cardiovascular disease. Fructose-induced insulin resistance may contribute a role in the present observation by impairing LDL receptor activity, thereby reducing hepatic uptake of circulating LDL-C, an assumption that aligns well with observations made by Basciano et al. (2005).

The differential effects observed among glucose, sucrose, and fructose can be attributed to their distinct metabolic pathways. While glucose metabolism is tightly regulated by insulin, fructose metabolism occurs largely independent of insulin control, allowing for continuous hepatic uptake and conversion into lipogenic substrates (Tappy, 2021). Sucrose, being a disaccharide composed of single units of both glucose and fructose, exhibits intermediate effects, as reflected in these findings. The enhanced dyslipidemic effect of fructose shown in this study is in line with mounting evidence that excessive fructose consumption is associated with development of cardiovascular illnesses, non-alcoholic fatty liver disease (NAFLD), and metabolic syndrome (Ter Horst and Serlie, 2017).

Conclusion

According to the study's results, Wistar rats' splenic lipid profile characteristics are considerably changed by long-term dietary consumption of glucose, sucrose, and fructose. Fructose had the most pronounced dyslipidemic effect, as seen by markedly elevated TC, TAG, and LDL-C levels together with decreased HDL-C levels. These findings imply that altered lipid balance in peripheral organs like the spleen may result from consuming excessive amounts of dietary carbohydrates, especially fructose. Further studies involving molecular, inflammatory, oxidative stress, and histopathological assessments are recommended to unravel the underlying mechanisms driving these observations.

Limitations

Although this research work demonstrates significant alterations in splenic lipid parameters following dietary sugar administration, the study is limited as the exact molecular mechanisms underlying these changes were not investigated and discussions were only adduced from established textbooks-styled literatures. Therefore, interpretations relating to insulin resistance, hepatic lipogenesis, oxidative stress, or inflammatory signaling in the context of splenic lipid metabolism warrant further investigation using molecular and histopathological approaches.

Project Declarations

(1) Funding

No funding in any form or manner was received for this study

(2) Competing Interest

There are no identifiable instance(s) that may compete or interfere with the intent and interpretation of the results reported in this study.

(3) Author's Contribution

- Akinade K. Adetola – Conceptualization, project investigation and preparation of manuscript
- Regina N. Ugbaja– Project supervision and monitoring,
- Basiru A. Salau – Project supervision and evaluation, proofing of manuscript
- Grace O. Ayorinde – Project supervision

(4) Acknowledgement

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