Journal of Bioscience and Biotechnology Discovery
Volume 8(5), pages 136-140, October 2023
Article Number: DA0F145D2
ISSN: 2536-7064
https://doi.org/10.31248/JBBD2023.195
https://integrityresjournals.org/journal/JBBD
Full Length Research

Effect of high-sucrose diet on liver enzymes and serum protein levels of Wistar albino rats

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Received 7th September 2023; Accepted 19th October 2023

ABSTRACT: A global change in dietary habits has led to the introduction of sweeteners in foods. This study investigated the effect of concentrations of sucrose on liver enzymes and serum protein levels in Wistar rats. Thirty-five (35) Wistar rats were equally randomized into seven groups and fed with a rat diet mixed with sucrose at concentrations of 10, 20, 40, 60, 80, and 100% w/w, while the control group was fed on a normal diet without sucrose. Their blood samples were analyzed for total protein, albumin, ALT, AST, ALK phosphatase, and gamma-glutamyl transpeptidase (ɣGT) levels. The results indicated that there was a significant ($p<0.05$) increase in AST (16.00-82.00 µ/L), ALT (44.00-90.80 µ/L), ALK Phos (44.00-90.80 µ/L), and a corresponding decrease in total proteins (69.80-61.39 g/L), albumin (36.00-34.00 g/L) and ɣGT (493.00-191.00 µ/L) levels as the concentration of sucrose increased. Rats fed with sucrose diets had higher levels of AST (39.27 µ/L), ALT (14.50 µ/L), and ALK Phos (68.47 µ/L) than rats fed with normal diets. Therefore, high doses of sucrose can cause increases in serum liver enzymes and total proteins that are suggestive of liver necrosis. Hence, by decreasing the concentrations of sucrose, the liver may be protected.

Keywords: Sucrose, rat, liver, protein, diet, enzymes.

INTRODUCTION

Sucrose is a disaccharide that contains 50% glucose and 50% fructose. It is both the chemical and common term for sweet, soluble carbohydrates, several of which are utilized in food. It is a naturally formed carbohydrate present in a variety of fruits, vegetables, and grains, but it is also incorporated into a variety of processed foods, including candy, ice cream, breakfast cereals, canned goods, soda, and other sugary drinks. Sucrose is frequently produced and processed for human use from either sugarcane or beet sugar (Jameel *et al.*, 2014). Sucrose intake rises in a nearly linear connection with plasma cholesterol (Zhou *et al.,* 2023). Increased very-low-density lipoprotein (VLDL) cholesterol has been linked to an increased risk of cardiovascular disease, which can be altered by a high-sugar diet (Vogel *et al.,* 2021). A high sucrose (>20%) energy diet is also linked to an increase in plasma triglyceride levels (Jo and Park, 2023).

The impacts of carbohydrates and fat on growth, weight gain, liver enzymes, and lipid metabolism have been examined (Welch-White *et al.,* 2013; Varani *et al.,* 2022), except carbohydrates on liver function indices. Studies by Fu *et al.* (2023) have demonstrated that rats fed a high sucrose diet (66.3%) had higher serum triglyceride and total cholesterol concentrations than rats fed with a normal diet.

The liver is the second largest organ in the body and is essential for maintaining systemic lipid homeostasis. It performs a variety of functions, including lipid and

carbohydrate metabolism, hormone production, clotting factor synthesis, and detoxification (Wei *et al*., 2022; Broadfield *et al*., 2021). Like many other organs, the liver's morphology is directly related to its function (Olurishe *et al*., 2011; Hazin *et al*., 2009). Significant changes in its anatomy or function may result in severe changes in its metabolic roles, which may hurt physiological functions. A two-to-threefold increase in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels is the most common abnormality in liver function tests (transaminases). They are linked to liver cell inflammation and/or injury, a condition known as hepatocellular liver injury (Kuraji *et al.,* 2021). Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) enzyme activities have been deemed significant markers of liver function in clinical practice (Guan *et al.*, 2021). Variations in ALT, AST, and ALP levels are primarily caused by enzyme leakage from hepatocyte cytosol into the bloodstream. While an increment in these enzyme activities in serum may imply severe liver disease, lower serum albumin (ALB) and total protein (TP) levels are also used as functional biomarkers because they may indicate abnormalities in the human system, protein synthesis and accelerated protein degradation in liver diseases (Zhang *et al*., 2022). As a result, understanding changes in liver functions requires knowledge of the pathophysiology of liver enzymes (Manimegalai *et al*., 2022).

Liver enzymes are the most common and least expensive paraclinical examination when monitoring liver status, even if they are not the most trustworthy inquiry for diagnosing disorders such as non-alcoholic fatty liver diseases (NAFLD) and non-alcoholic steatohepatitis (NASH) (Fang *et al.*, 2023). They are less expensive than radiologic procedures such as ultrasound scanning, computed tomography scanning, or magnetic resonance scanning (MR scan) of the liver. They are also less intrusive than a liver biopsy, which is the only sure technique to diagnose a specific liver illness (Fang *et al.*, 2023). As a result, liver enzymes are evaluated in a variety of clinical settings.

Serum liver enzymes are primarily found within liver cells. When the liver is injured or damaged, the liver cells release these enzymes into the bloodstream, raising their levels and signaling liver disease (Ibukun, 2023). Total protein and bilirubin may also be involved in human and animal liver function. The ability of a high sucrose diet to cause changes in serum liver enzymes, total protein, and albumin levels in Wister rats *in vivo*, thus determining its safety at different concentrations, will be studied in this study.

MATERIALS AND METHODS

Materials

Thirty-five (35) Wistar albino rats with 0.195 kg average body weight were obtained from the animal house of the Department of Pharmacology and Toxicology, University of Port Harcourt. The rats were acclimatized to laboratory conditions for 14 days before the commencement of the study and fed *ad libitum* with normal rat feed and water. Commercially prepared Alanine aminotransferase, aspartate aminotransferase, total protein, and albumin reagents were obtained from Randox Diagnostics, London, while alkaline phosphatase and gamma-glutamyl transpeptidase reagents were obtained from Quimica Clinica Aplicada (QCA) Spain.

The test animals were divided into seven groups of five test animals per group and fed with rat diet mixed with sugar at concentrations of 10, 20, 40, 60, 80, and 100% w/w, while the last group was fed normal rat diet with distilled water to serve as a control (0.00 g/kg) for three weeks. The animals were sacrificed by cervical incision, and blood was collected into test tubes by cardiac puncture, into EDTA-coated test tubes (Madaki *et al*., 2021), and taken to the laboratory for analysis (Moniruzzaman *et al.,* 2012).

Biochemical analysis

ALT was measured by monitoring the concentration of pyruvate hydrazone formed with 2, 4, dinitrophenylhydrazine (Dhakad *et al*., 2019). Alkaline phosphate (Alk Phos) level was determined by the phenolphthalein monophosphate method as described by Brufsky *et al*. (2020). Gamma-glutamyl transpeptidase (ɣGT) level was determined using the modified Szasz method (Oyesola *et al*., 2022). Aspartate aminotransferase was measured by monitoring the concentration of pyruvate hydrazone formed with 2, 4, dinitrophenylhydrazine (Dhakad *et al*., 2019).

The total protein level was determined by the biuret method (Okpoghono *et al*., 2023). The measurement of serum albumin was based on its quantitative binding to the indicator 33'55' tetra Bromo-m cresol sulphone-phthalein (bromocresol green BCG). The albumin BCG – complex absorbs maximally at 578 nm, the absorbance being directly proportional to the concentration of albumin in the sample (Elafify *et al*., 2023). External quality control sera were assayed along with the analyses.

Ethical considerations

The experimental protocol was approved by the Animal Care and Ethics Committee of the University of Port Harcourt and was by guidelines provided by the Nigerian National Health and Medical Research Council.

Statistical analysis

The biochemical data were subjected to statistical analysis such as mean (X), standard deviation (SD), and standard

Table 1. Effect of sucrose concentration on liver enzymes and proteins.

Sucrose conc. (%)	Total proteins (g/L)	Albumin (g/L)	AST (U/L)	ALT (U/L)	Alkaline Phos. (U/L)	ɣGT (U/L)
0.00	69.80±1.80^{a}	36.00±1.76^{a}	16.00±2.56^{d}	10.00±1.94^{d}	44.00±3.56^{e}	493.00±59.45^{a}
10%	65.60±2.48^{b}	34.60±1.54^{b}	16.00±2.68^{d}	10.60±2.31^{d}	48.00±7.60^{e}	382.00±63.52^{b}
20%	63.50±1.70^{c}	34.41±0.84^{b}	18.00±2.58^{d}	10.80±0.92^{d}	58.00±4.77^{d}	373.00±90.30^{c}
40%	64.71±1.58^{bc}	34.25±1.10^{b}	19.00±3.25^{d}	13.40±0.96^{c}	58.610±5.99^{d}	232.40±70.45^{d}
60%	62.22±2.66^{cd}	34.17±1.05^{b}	28.00±5.85^{c}	13.80±1.85^{c}	84.00±5.99^{c}	235.00±28.91^{d}
80%	61.39±1.73^{d}	34.00±1.30^{b}	82.00±4.77^{b}	15.60±1.02^{b}	76.00±17.16^{b}	228.00±31.61^{e}
100%	61.92±3.49^{d}	34.08±1.92^{b}	74.00±4.92^{a}	24.80±2.65^{a}	90.80±4.49^{a}	191.00±18.28^{f}
T	4.307	1.002	52.005	9.067	3.508	382.8
P	0.003	0.443	0.000	0.000	0.010	0.007

Mean values are of duplicate determinations. Mean values within a column with different superscripts are significantly different at ($p < 0.05$). P= Probability level T= T-test

Table 2. Effect of sucrose diet on liver enzymes and proteins.

Parameter	Control	Sucrose	t	P
Total Protein (g/l)	69.80±1.80^{a}	67.60±1.24^{b}	67.91	0.003
Albumin (g/l)	36.10±1.76^{a}	36.00±0.56^{a}	36.09	0.443
AST(U/l)	18.00±2.59^{a}	39.27±5.38^{b}	36.23	0.000
ALT(U/l)	10.00±1.95^{a}	14.50±1.16^{b}	13.86	0.000
Alkaline Phosphatase (U/l)	48.00±7.60^{a}	68.47±4.80^{b}	65.54	0.010
ɣGT (U/l)	493.00±59.45^{a}	273.57±25.26^{b}	3.05	0.007

Mean values are of duplicate determinations. Mean values within a column with different superscripts are significantly different at ($p < 0.05$).

error of the mean (SEM), while analysis of variance (ANOVA) was used to test for differences between treatment groups using Statistical Package for Social Sciences (SPSS) version 16. A value of $p<0.05$ was accepted as significant.

RESULTS

As represented in Table 1, the total protein and albumin concentrations and serum liver enzyme activity in Wistar rats administered graded concentrations of sucrose were studied. Total protein and albumin levels of the Wistar rats after administration of sucrose ranged from 61.91-69.80 g/L and 36.00-34.00 g/L, respectively. The highest concentration was found in Wistar rats fed with the control diet, while the lowest concentration was found in Wistar rats fed with 80% sucrose. AST, ALT, ALK Phosphatase levels ranged from 16.00-82.00, 10.00-24.80, and 44.00-90.80 U/L, respectively. There was a significant ($p<0.05$) increase in the enzyme levels (AST, ALT, and ALK phosphatase) as the concentration of sucrose increased. The highest ALT and AKP Phosphatase concentrations were found in Wistar rats fed with 100% sucrose, while the highest AST level was found in Wistar rats fed with 80% sucrose. There was a significant ($p<0.05$) decrease in ɣGT level following an increase in the concentration of sucrose. The values ranged from 191.00-493.00 U/L, with the highest level found in Wistar rats fed with 100% sucrose, while Wistar rats fed with a control diet had the lowest ɣGT level. Also, in Table 2, Wistar rats fed with a control diet had high concentrations of total proteins (69.80 g/l), albumin (36.10 g/L), and ɣGT level (493.00 U/L), while Wistar rats fed with sucrose diet had showed higher levels of AST (39.27 U/L), ALT (14.50 U/L), and ALK Phosphatase, (68.47 U/L).

DISCUSSION

In this study, an increase in the concentration of sucrose led to a significant decrease in total proteins and albumin levels. However, this difference was not significant for the albumin level. Total proteins (albumin) are produced by the liver, and in the case of liver damage, production of these proteins is reduced or completely ceased. The concentrations of the total protein and albumin in this study may indicate the state of the liver and the type of damage (Ajakaiye *et al*., 2022).

Liver enzymes, AST, ALK Phosphatase, and ALT, were elevated across all treatment groups. The normal ranges of ALT and AST are 17.5 – 30.2 U/L and 45.7 – 80.8 U/L, respectively. ALT levels were significantly highest among rats fed 40 - 100% sucrose diets, while AST was signify-

cantly highest among rats fed with 60-100% sucrose compared to the control rats ($p< 0.05$). The elevation of these liver enzymes values may be indicative of some liver impairments or possible damage. Liver damage resulting from underlying cellular death is often associated with cholestasis, drug-induced injury, and obesity (Fernández *et al.,* 2012). The liver is intricately connected to lipid metabolism as well as to the maintenance of homeostasis. The findings of this study revealed increased ALT and AST values; this may suggest that the role of sucrose influences the levels of these transaminases. Although this study is the first to investigate the influence of sucrose diets on liver enzymes and serum proteins, other studies have reported an increase in liver enzymes following administration with high fat and cholesterol diets. Panchal *et al.* (2011) evaluated high-fat/high-cholesterol diets and reported increased liver weight, fat deposition, inflammation, and fibrosis with increased plasma activity of liver enzymes. Karacor *et al*. (2014) investigated the role of a high-fat diet on weight gain and its effects on the liver. They reported that ALT levels in the high carbohydrate diet group of rats at 16 weeks were significantly higher in biochemical evaluation than in the control group. They further reported that a diet rich in carbohydrates has adverse effects on the liver. Petrikova *et al*. (2020) also found out that a high carbohydrate, low-fat diet led to hypertriglyceridemia, as an indicator of hepatocellular injury, reduced serum protein, and increased AST, ALT, and urea levels (Sato *et al*., 2022). Also, it was determined that a high carbohydrate diet increased hepatic fat synthesis, led to the accumulation of triglycerides in the liver, raised ALT, and AST levels, and caused mitochondrial dysfunction in adipose tissue (Myers *et al.,* 2022; Ozkan *et al.,* 2019).

There was also a significant increase in the ALK Phosphatase activities at higher levels of sucrose administration. Alkaline phosphatase is a hydrolytic enzyme that is responsible for the removal of phosphate groups from many including nucleotides and proteins. ALP is particularly concentrated in the liver, bile duct, kidney bone, and placenta. An increase in ALP may indicate an obstruction of the bile duct and may consequently affect the liver site. An increase in ALP may also be a result of celiac disease (Chukwudoruo *et al*., 2021). Alanine transaminase usually increases where the liver has been diseased or damaged (Niemela *et al*., 2023) and is also a test used for screening liver problems. Aspartate transaminase is a commonly measured clinical marker for liver health (Niemela *et al*., 2023). Hence, the increased level of the liver serum enzyme may indicate enzyme activity observed in this study at high levels of administration of sucrose indicating possible hepatotoxicity at high doses.

Conclusion

This study has shown that levels of liver enzymes, AST, ALT, and ALK-Phosphatase increased after 3 weeks' high-sucrose diet group while total proteins, albumin, and ɣGT levels decreased. Therefore, it could be concluded that low concentrations of sucrose could protect the liver.

COMPETING INTEREST

The authors state that they have no known competing interests or personal ties that could appear to have influenced the work described in this study.

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