

The Effect of Sugar Type on Blood Glucose Levels and Selected Biochemical Parameters in Experimental Animals

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Abstract: While the adverse effects of refined sugars on metabolic health have been widely investigated, data on the metabolic impact of certain natural and artificial sweeteners remain limited. This study aimed to compare the metabolic responses to the consumption of stevia sugar and high-fructose corn syrup (HFCS) relative to a standard diet in rats by assessing key metabolic indicators, including weight gain, food intake, feed conversion efficiency, blood glucose levels, and plasma lipid profiles. The results showed that rats fed a stevia-supplemented diet exhibited the lowest weight gain compared to the control group, with a statistically significant difference, whereas the HFCS-fed group demonstrated a significantly higher weight gain than the control. In terms of food consumption, the stevia group recorded the lowest intake, while the HFCS group had the highest intake among all experimental groups. The feed conversion efficiency was highest in the HFCS group, indicating greater efficiency in converting food intake into body weight gain compared to the control, whereas the stevia-fed group had significantly lower feed conversion efficiency, suggesting reduced efficiency in weight gain. Furthermore, HFCS consumption led to a significant increase in plasma glucose levels, whereas stevia consumption resulted in a significant reduction in plasma glucose compared to the control. Regarding lipid profile, stevia consumption did not cause significant alterations in total cholesterol or triglyceride levels, but it led to a significant reduction in these parameters compared to HFCS consumption. Conversely, HFCS consumption significantly elevated total cholesterol and triglycerides, accompanied by a notable decrease in HDL and a significant increase in LDL and VLDL compared to the control, highlighting its detrimental effects on lipid metabolism.

Keywords: Carbohydrate metabolism, stevia sugar, high-fructose corn syrup, blood glucose, plasma lipids.

INTRODUCTION

Obesity is a global epidemic associated with numerous metabolic disorders (1), including elevated blood glucose levels, increased plasma lipids, and changes in body weight, all of which contribute to a higher risk of developing metabolic syndrome (MetS) (2), non-alcoholic fatty liver disease (NAFLD), type 2 diabetes (T2D), and cardiovascular disease (CVD) (3). These metabolic disturbances have been linked to changes in dietary habits and lifestyle (4), particularly with the increasing consumption of added sugars and diets rich in refined carbohydrates and fats, which are typically low in fiber. Excessive intake of added sugars has been shown to play a key role in obesity (2)(5), prompting several health organizations to recommend reducing sugar consumption (6). However, limiting sugar intake poses a significant challenge, as many processed foods and beverages contain large amounts of added sugars, such as sucrose, glucose, and fructose (7)(8). In this context, fructose has emerged as a primary component of added sugars (9). Studies have demonstrated that excessive fructose consumption can lead to metabolic disturbances, including elevated blood glucose levels, increased triglycerides and cholesterol, and weight gain, making it a major contributor to obesity-related health issues (2)(5)(10). While research has extensively highlighted the negative effects of refined sugars, growing attention has been directed toward alternative sweeteners, both natural and artificial, which may offer potential health benefits compared to sucrose and high-fructose corn syrup (HFCS) (11). Stevia sugar is a low-calorie artificial sweetener that is believed to have a lesser impact on blood glucose and lipid levels.

Some studies have suggested that stevia may play a role in reducing weight gain, making it a potential option for mitigating the adverse effects of added sugars (12)(13)(14).

EXPERIMENTAL DESIGN

The experiment was approved by the Scientific Research Ethics Committee at the Iraqi Ministry of Higher Education and Scientific Research – University of Kufa. This study utilized Albino Wistar rats with an initial body weight ranging between 111–157 g, randomly assigned into three groups of eight rats each, totaling 24 rats. The animals were housed in a temperature- and humidity-controlled environment with a 12:12-hour light-dark cycle, with the light period starting at 07:00 AM. After a one-week acclimatization period, during which all rats were fed a standard diet, they were divided into three dietary groups: the first group, which served as the control, was fed a standard diet, while the second group received a diet supplemented with stevia sugar, and the third group was fed a diet containing high-fructose corn syrup (HFCS). At the end of the experimental period, the rats were fasted, and blood samples were collected via cardiac puncture into anticoagulant-treated tubes for subsequent biochemical analysis of metabolic indicators.

Growth Indicators of Experimental Animals

The body weights of the experimental animals were measured using a single-pan balance once per week to monitor weight gain. The following growth indicators were calculated according to the method described by (15):

$$\text{Weight Gain} = \text{Final Body Weight} - \text{Initial Body Weight}$$

$$\text{Feed Efficiency Ratio (FER)} = \text{Weight Gain} / \text{Food Intake}$$

Food Intake

The rats were provided with feed quantities determined based on their body weight, and the remaining feed for each group was recorded daily. The food intake was calculated using the following equation, as described by (16):

$$\text{Food Intake} = \text{Total Feed Provided (g)} - \text{Remaining Feed (g)}$$

Measurement of Fasting Blood Glucose Levels

Fasting blood glucose levels in rats were monitored and measured twice per week throughout the experiment to assess hyperglycemia. Blood samples were collected from the tail vein, and glucose levels were determined using an Accu-Chek glucose meter, following the method described by (17).

Estimation of Total Cholesterol and High-Density Lipoprotein (HDL) Concentration in Serum

The enzymatic hydrolysis method was used to determine total cholesterol levels, employing a commercial assay kit manufactured by Bio Research, as described by (18).

Estimation of Triglyceride (TG) Concentration in Serum

The concentration of triglycerides (TG) in serum was determined enzymatically following the method described by (19).

Estimation of Low-Density Lipoprotein (LDL) and Very Low-Density Lipoprotein (VLDL) Levels in Serum

The concentrations of low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) in serum were calculated using Friedewald's equation, as described by (20), using the following formulas:

$$\text{VLDL-C} = [\text{Triglyceride} / 5]$$

$$\text{LDL-C} = [\text{Total Cholesterol}] - [\text{HDL} + \text{VLDL}]$$

RESULTS

The results indicate clear differences in final body weight and weight gain among the groups. Rats that consumed the high-fructose corn syrup (HFCS)-supplemented diet exhibited the highest weight gain compared to the other groups, whereas the stevia-fed group showed significantly lower weight gain. Although food intake did not differ significantly among the groups, feed efficiency was lower in the stevia-fed group compared to both the control and HFCS-fed groups, suggesting that the type of sugar used influences the efficiency of food conversion into body mass. Compared to the control group, HFCS consumption resulted in a higher weight gain rate, reflecting the impact of this sugar type on energy metabolism and fat storage (21). Conversely, rats in the stevia group exhibited the lowest weight gain, which may indicate a potential effect of stevia in reducing appetite (22). Despite the lack of significant differences in food intake, feed efficiency varied considerably, being higher in the HFCS group than in the stevia group. The results also demonstrated that food intake was highest in the HFCS-fed group, which also exhibited a high feed efficiency ratio, suggesting that HFCS enhances the body's ability to convert food into weight gain. These findings align with those of (23), who reported that sugars such as fructose result in a weak response to satiety hormones, including GLP-1 and PYY, thereby reducing their appetite-suppressing effects and leading to increased food intake. Similarly, (24) supports these results, demonstrating that fructose-containing sugars affect the activity of AgRP neurons, which stimulate appetite and contribute to increased food consumption. In contrast, the stevia-fed group recorded the lowest food intake and feed efficiency compared to the other groups, which is consistent with the findings of (25), who observed that stevia consumption reduces hunger without subsequent compensatory food intake. This can be attributed to the fact that stevia does not provide energy in the same manner as other sugars, leading to a lower weight gain rate in this group (26)(27). The effect of HFCS on weight gain is attributed to the metabolic nature of fructose, which is rapidly converted into triglycerides in the liver, resulting in fat accumulation and increased body weight (21)(28). Additionally, fructose consumption alters the balance of appetite-regulating hormones, as it reduces leptin secretion, the hormone responsible for satiety, while increasing ghrelin levels, which stimulate appetite, ultimately promoting higher food intake and subsequent weight gain (29).

Table 1: Effect of Sugar Type on Body Weight, Growth Rate, and Feed Intake

Parameter	Control Group (Standard Diet)	Stevia Group	HFCS Group
Initial Body Weight (g)	142.5a ± 5.529	144.0a ± 5.182	145.0a ± 15.31

Final Body Weight (g)	206.2b ± 12.57	190.1a ± 9.583	218.6b ± 15.86
Weight Gain (g)	63.7	45.1	74.6
Growth Rate (g/day)	2.12	1.5	2.48
Feed Intake (g/day)	2401	2256	2698
Feed Efficiency Ratio (FER)	0.212	0.159	0.232

Values are expressed as the mean ± standard deviation (SD) for eight replicates. Different letters within the same row indicate statistically significant differences at ($P < 0.05$) according to Duncan's test.

This table provides a comparative analysis of body weight, growth rate, feed intake, and feed efficiency in rats subjected to different dietary sugar sources, highlighting significant metabolic differences among the groups.

Blood Glucose Levels

The results presented in Figure 1 indicate significant differences in blood glucose levels among the experimental groups, with the HFCS group exhibiting the highest glucose level, followed by the control group, while the stevia group recorded the lowest glucose level. The stability of blood glucose levels in the control group reflects the nutritional balance of the standard diet, which helps maintain normal glucose homeostasis. The stevia group showed a significant reduction in blood glucose levels compared to the other groups, which may be attributed to the phenolic compounds in stevia, known to inhibit hepatic glucose production, enhance glucose uptake in cells, stimulate insulin secretion, and slow down glucose absorption in the intestine. These findings align with previous reports by (30) and (31). Conversely, the HFCS group exhibited a significant increase in blood glucose levels compared to all other groups, likely due to fructose's role in downregulating glucose metabolism-related genes in the pancreas, leading to reduced insulin secretion. Additionally, a portion of fructose is converted into glucose in the liver, increasing the glucose burden in the bloodstream. These results are consistent with the findings of (32) and (33).

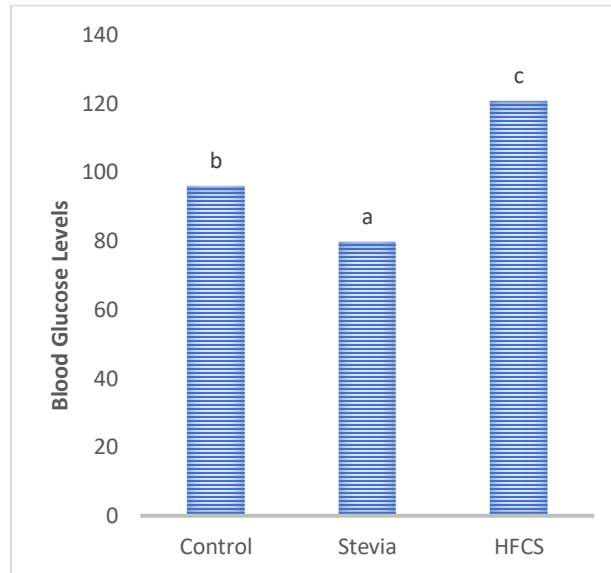


Figure 1: Blood Glucose Levels in Experimental Animals (mg/dL)

Values are expressed as the mean for eight replicates. Different letters indicate statistically significant differences at ($P < 0.05$) according to Duncan's test

Total Cholesterol Level

The results, as illustrated in Figure 2, indicate significant differences among the three experimental groups. The control group exhibited normal total cholesterol levels, reflecting the body's ability to regulate cholesterol balance under a balanced diet, as reported by (34). In contrast, the stevia group showed a significant reduction in total cholesterol levels compared to the control, which is consistent with the findings of (35). This reduction is attributed to stevia's role in lowering cholesterol levels by enhancing bile acid excretion, thereby promoting the elimination of excess cholesterol (36). Conversely, the HFCS group exhibited a significant increase in total cholesterol levels compared to the other groups, highlighting its lipogenic effect and its role in increasing very low-density lipoprotein (VLDL) production. This effect is attributed to fructose's ability to stimulate de novo lipogenesis in the liver, leading to increased fat accumulation and elevated cholesterol secretion into the bloodstream (37).

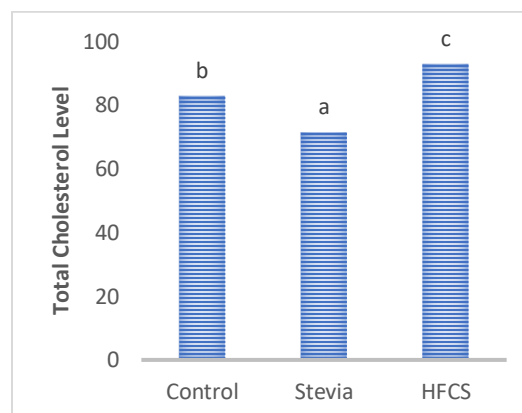


Figure 2: Total Cholesterol Levels in Experimental Animals (mg/dL)

Values are expressed as the mean for eight replicates. Different letters indicate statistically significant differences at ($P < 0.05$) according to Duncan's test

Triglyceride Levels

Statistical analysis revealed significant differences among the groups, with triglyceride levels being lower in the stevia group compared to both the control and HFCS groups. This reduction may be attributed to stevia's ability to enhance bile acid excretion and reduce its reabsorption, thereby limiting triglyceride accumulation in the bloodstream (39). In contrast, the HFCS group exhibited a significant increase in triglyceride levels compared to both the control and stevia-fed groups, indicating enhanced hepatic lipogenesis and increased triglyceride synthesis (37).

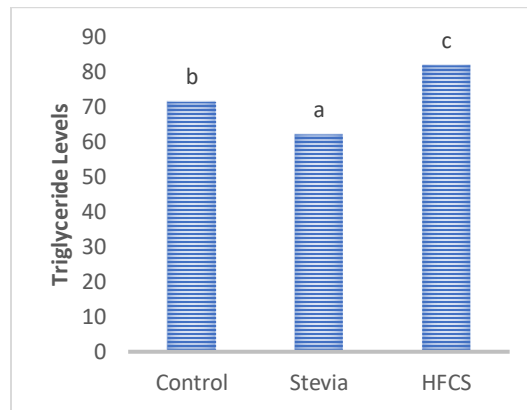


Figure 3: Triglyceride Levels in Experimental Animals (mg/dL) Values are expressed as the mean for eight replicates. Different letters indicate statistically significant differences at ($P < 0.05$) according to Duncan's test

HDL Levels

The analysis showed that HDL-C levels were highest in the stevia group compared to the other groups, as illustrated in Figure 4. The control group recorded 38.05 mg/dL, while the HFCS group recorded 32.47 mg/dL, indicating that stevia supplementation significantly increased HDL-C levels compared to both the control and HFCS groups. Conversely, the HFCS group exhibited a significant reduction in HDL-C levels compared to the other groups. The increase in HDL-C levels in the stevia group may be attributed to the effect of steviol glycosides in stimulating lecithin-cholesterol acyltransferase (LCAT) activity, an enzyme responsible for cholesterol transport from tissues to the liver for excretion, thereby promoting higher HDL-C levels in the bloodstream (36)(39). These findings are consistent with the results of (40), who reported that stevia consumption enhances lipid metabolism and improves insulin sensitivity, contributing to elevated HDL-C levels. In contrast, the HFCS group exhibited a significant decline in HDL-C levels, further demonstrating its negative impact on lipid metabolism.

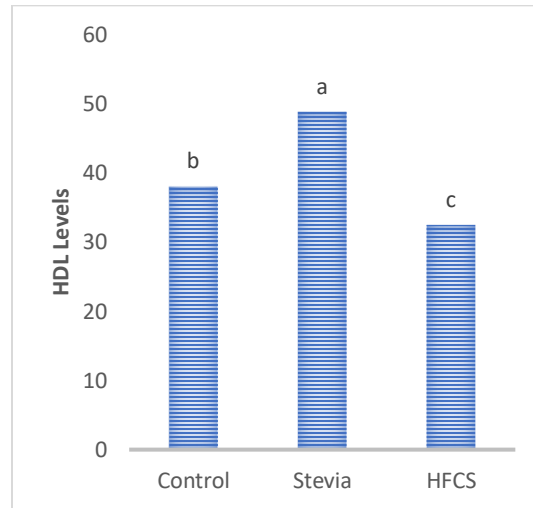


Figure 4: HDL Levels in Experimental Animals (mg/dL)

Values are expressed as the mean for eight replicates. Different letters indicate statistically significant differences at ($P < 0.05$) according to Duncan's test

LDL Levels

The results presented in Figure 5 illustrate the differences in LDL-C levels among the experimental groups, with the control group recording 30.48 mg/dL, the stevia group 10.19 mg/dL, and the HFCS group 44.00 mg/dL. These findings indicate that stevia supplementation significantly reduced LDL-C levels compared to both the control and HFCS groups. The marked reduction in LDL-C levels in the stevia group may be attributed to stevioside's role in stimulating hepatic LDL receptors, which enhances LDL-C uptake from the bloodstream, thereby lowering its concentration (36). This is supported by (41), who reported that stevia consumption resulted in a significant reduction in triglycerides and LDL-C levels, leading to a decrease in VLDL-C levels in blood plasma. This effect is likely due to stevia's antioxidant properties, which help reduce oxidative stress and improve lipid metabolism (41). Conversely, the HFCS group exhibited a significant increase in LDL-C levels, which may be attributed to fructose-induced de novo lipogenesis (DNL) in the liver, leading to increased triglyceride production and hepatic fat accumulation. Additionally, fructose may reduce the activity of peroxisome proliferator-activated receptor alpha (PPAR α), thereby decreasing fatty acid oxidation and promoting fat accumulation. Furthermore, fructose consumption may inhibit the activity of microsomal triglyceride transfer protein (MTP), impairing the export of triglycerides via very low-density lipoproteins (VLDL), resulting in their hepatic accumulation. Moreover, fructose may downregulate hepatic LDL receptors, limiting the body's ability to clear LDL-C from the bloodstream, leading to its elevated circulation levels (42).

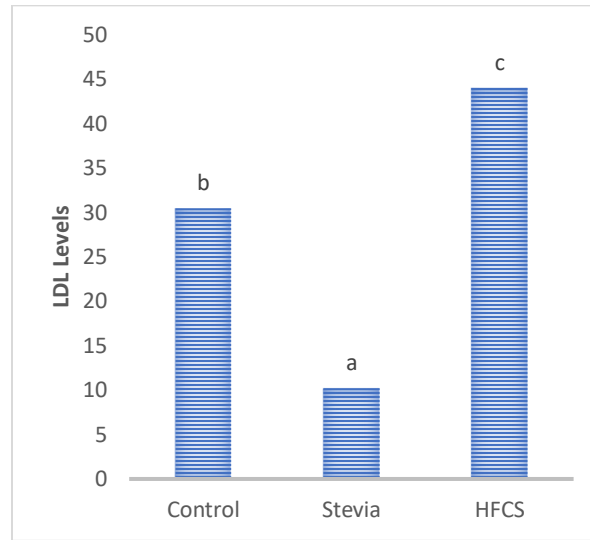


Figure 5: LDL Levels in Experimental Animals (mg/dL)

Values are expressed as the mean for eight replicates. Different letters indicate statistically significant differences at ($P < 0.05$) according to Duncan's test

VLDL Levels

As illustrated in Figure 6, significant differences in VLDL-C levels were observed among the experimental groups. The control group recorded 14.06 mg/dL, the stevia group 12.30 mg/dL, and the HFCS group 16.43 mg/dL. These findings indicate that the stevia-supplemented group exhibited a significant reduction in VLDL-C levels compared to both the control and HFCS groups, while the HFCS group showed a significant increase compared to the other two groups. The notable reduction in VLDL-C levels in the stevia group may be attributed to its ability to reduce hepatic triglyceride synthesis, thereby lowering VLDL-C concentrations in the bloodstream (41). Conversely, the HFCS group exhibited a significant increase in VLDL-C levels, reflecting its lipogenic effect and its role in enhancing triglyceride production and VLDL secretion (43). It has been reported that fructose consumption stimulates hepatic lipogenesis, leading to increased VLDL-C production and elevated plasma levels (44).

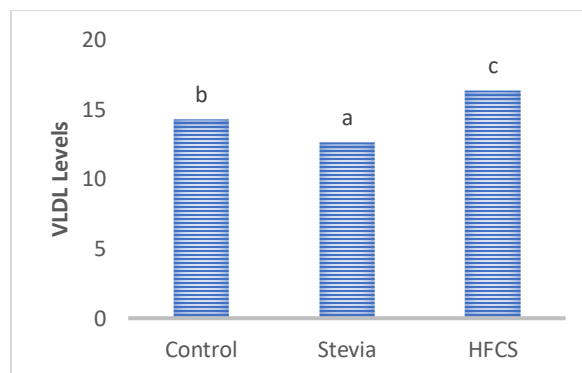


Figure 6: VLDL Levels in Experimental Animals (mg/dL)

Values are expressed as the mean for eight replicates. Different letters indicate statistically significant differences at ($P < 0.05$) according to Duncan's test

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