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The Effect of Artificial Sweetener "Cipla" on Liver Function in Diabetic Male Rats

Ramin Ghasemi[1], **Jafar Rahmani Kahnamooi**[1*]

Abstract

Objectives: Sucralose is an artificial sweetener of sucrose, which is 600 times sweeter than sugar and produces low calories. Cipla is a commercial sweetener, which has sucralose and other various constituents. The present study evaluated the effects of Cipla on some biochemical factors of rats.

Materials and Methods: The study was done on 24 male rats, which was randomly distributed to 4 groups of healthy control, diabetics control, treatment healthy, and diabetics treatment. Healthy and diabetic control groups were fed with a base diet. Healthy and diabetics treatment groups received sucralose through gavage 15 mg/kg daily for a month. Then, streptozotocin was administered intra-peritoneally (65 mg/kg one dose) to induce diabetes. At the end of the study, albumin, bilirubin, total protein, alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP) of the serum were evaluated and the results were analyzed by SPSS 22.

Results: The results indicated that the total proteins of the serum, albumin, and bilirubin, ALT, AST, and ALP were not different statistically in different groups ($P>0.05$).

Conclusions: In general, it was found that Cipla as a sweetener has not any side effects and has no negative effects on the liver function of the rat.

Keywords: Cipla, Sucralose, Serum biochemical parameters, Rat, Liver function

Introduction

In the carbohydrate metabolism, the liver has an important role and regulates the blood glucose by glycogenesis and glycogenolysis (1,2). The prevalence of diabetes is increasing in developing countries and it is expected that the prevalence of type 2 diabetes increases explosively (3). Currently, diabetes is incurable, and the glycemic should be controlled to delay the complications (4). Nonnutritive sweeteners have a role in glycemic control (5). Sweeteners are classified into four main natural, artificial, purified, and sugar-alcohol groups. The consumption of these substances increases, along with the appearance of the sugar industry and the production of various purified sweeteners. However, the spread of other metabolic disorders, obesity, cardiovascular disease, and diabetes due to inevitable changes and the lifestyle of humans has led humans to substitute it with artificial sweeteners (6).

These substances do not produce much energy and some are defecated without entering the metabolic process. The production of these substances facilitates the production of soft drinks, chocolates, and diet jams for the consumption of diabetics and obese people while the main problem for consuming these substances is their potential health risks to human beings. These substances should be used as additives in the food industry after the approval and ratification of usage in foodstuff (7). In this study, a non-sugar sweetener Cipla was used consisting mostly of sucralose, which is the only calorie-free sweetener and is derived from sugar and is 600 times sweeter than sugar (6,8,9).

The replacement of three molecules of chlorine makes sucralose, like sugar, unbreakable or metabolized. Therefore, sucralose quickly passes through the body without changing and is considered as an inert and safe substance (10).

Sucralose was first discovered in 1976 and then approved by the Food and Drug Administration (FDA) in 1998 (9,11). It is easily soluble in water and could be used in cooking due to its excellent durability.

In addition, sucralose tastes like sugar, which is completely understandable and does not have a pleasant taste. Further, sucralose is sweet and its sweetness remains in the mouth and causes no unpleasant taste (11). So far, no documented report has been reported for the adverse complications of this substance, including dental decay, increased sugar among diabetics, genetic changes, cancer, immunologic problems, central nervous system and environmental disorders, and birth defects (12,13).

The commercial sweetener (Cipla) was used in this study because it contains 6.5 mg lactose, cellulose, and magnesium stearates in addition to sucralose and has low calorie. The current study investigated the effect of artificial sweeteners on the liver function in diabetic and healthy rats.

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[1]Department of Clinical Sciences, Tabriz Branch, Islamic Azad University, Tabriz, Iran.
*Corresponding Author: Jafar Rahmani Kahnamooi, Email: Jrahmani28@gmail.com

Materials and Methods

This study was performed on 24 male rats that were randomly divided into 4 groups of healthy control, diabetic control, healthy treatment, and diabetic treatment. The diets of healthy control and diabetic control groups were the same. The dosage of sucralose was determined based on the standards available on the FDA website, which mentioned the sucralose acceptable daily intake up to a maximum of 15 mg/1 kg body weight for human beings (14). Therefore, the dose of Cipla was determined as 15 mg/kg and prescribed daily for one month to healthy and diabetic treatment groups by the gavage technique.

To have diabetic rats, 65 mg/kg streptozotocin dose was injected intraperitoneally and the serum glucose level was measured after 24 and 72 hours using a glucometer, and 240 mg/dL higher levels were considered as the diabetic rat.

During the experiment period, all rats had the same environmental conditions such as light, heat, and nutrition (14). At the end of the study, the bloodletting was conducted via euthanasia, anesthesia with ether, and the truncation of all rats under identical conditions. At the end of the experiment, blood samples were taken from the vein of the tail with ethical issues. Then, serum biochemical parameters were evaluated using Pars Azmoon kits and spectrophotometric methods with a 911 plus HITACHI auto analyzer. The data were analyzed by SPSS, version 22 through ANOVA and Tukey post hoc tests.

Results

The results indicated no significant differences between the groups regarding the tested parameters. However, the highest levels of total protein, albumin, and alkaline phosphatase (ALP) were observed in healthy treatment and healthy control groups ($P>0.05$). In addition, the highest aspartate transaminase (AST) levels were found in healthy treatment and diabetic control groups ($P>0.05$). Eventually, the highest alanine transaminase (ALT) and bilirubin levels were observed in the diabetic control group, diabetic treatment, and healthy treatment while the lowest levels were found in the healthy control group ($P>0.05$).

Discussion

Artificial sweeteners are globally used as a substitute for sugar in various types of foodstuff and beverages, as well as medicines and health products such as oral detergents. These sweeteners have no energy or produce slight energy and, for the same reason, are considered as one of the ingredients of nutritional products (15). In 2009, sucralose accounted for 16% of the sweetener market in the United States, and their consumption level increased by 5% annually (16). Sucralose is produced by the chlorination of sucrose, which creates a stable compound that is absorbed in the mammalian digestive system very slightly. The present study sought to evaluate the effect of using Cipla sweetener on serum biochemical parameters.

The researchers represented that the use of sucrose sweetener (Steviol) significantly increased total serum protein levels in hamsters. The activity level of AST and ALT also increased slightly. The researchers further emphasized that the increased levels of AST and ALT could be due to a defect in the plasma membrane of the liver cells leading to the leakage of these enzymes into the bloodstream. They also reported that the use of the sweeteners has caused the swelling of hepatocytes and thus their cytoplasm vacuole (17). Finally, the researchers found that fructose can increase uric acid in humans and animals (18,19). It has been also stated that an increase in serum uric acid is related to the incidence of cirrhosis and increased gamma-glutamyl transferase (GGT) and ALT activity (20). The activity of ALT and GGT and, to some extent, AST is a strong predictor of the metabolic syndrome and as a marker or non-alcoholic fatty liver disease person (21,22). The results of a study indicated that the use of fructose in a limited period is not effective on the level of AST and ALT (21). Moreover, the results of another study showed that the use of fructose for 10 weeks did not alter the level of AST and ALT (23).

Similarly, the results of previous research on the effect of aspartame on the amount of alkaline phosphatase demonstrated that there was no significant change in ALP levels following the use of aspartame (24). Researchers indicated that there was a significant increase in ALT, AST, and ALP levels in rats that received aspartame at 1000 mg/kg of bodyweight in the drinking water for 180 days. Therefore, they concluded that the long-term use of aspartame could lead to cellular damage in the liver and result in a change in the liver antioxidant status (25). Based on the findings of another study, using sucrose over 45 and 90 days caused a significant increase in alkaline phosphatase levels while alkaline phosphatase was

Table 1. Mean and Standard Error of Tested Parameters

Group	Total Protein (g/dL)	Albumin (g/dL)	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	Bilirubin (mg/dL)
Healthy control	7.20±0.06	3.36±0.11	78.20±10.29	18.80±2.03	462.80±90.56	0.14±0.02
Diabetic group	6.81±0.37	3.23±0.17	103.66±11.33	23.83±2.48	409.00±55.91	0.16±0.03
Healthy treatment	7.20±0.22	3.38±0.12	107.66±6.77	21.50±3.01	436.83±59.31	0.15±0.02
Diabetic treatment	6.85±0.19	3.15±0.21	76.50±5.73	22.25±2.32	392.50±24.54	0.15±0.05
P value	0.593	0.716	0.058	0.587	0.889	0.942

Note. AST: aspartate transaminase; ALT: alanine transaminase; ALP: alkaline phosphatase.

not affected by aspartame. On the other hand, sucrose significantly decreased ALT while it significantly increased AST in the rats compared to the control group (26).

The results of the present study indicated that the serum AST, ALT, and ALP levels were not statistically significant in the studied groups, representing the lack of the effect of Cipla sweetener on the above-mentioned parameters and the liver.

Other researchers reported that the increased total serum protein resulting from the use of sucrose sweetener was probably due to dehydration in hamsters, which was due to increased peritoneal fluid (17). It seems that stevia causes damage to mesenteric blood vessels and causes plasma fluid leaks into the peritoneum cavity. Based on the results of another research, the use of sucrose in rats did not affect the total serum protein content during 45 and 90 days after the study (26).

Based on the results of the present study, using Cipla had no significant effect on the total serum protein in different groups, which is consistent with the findings of some previous studies (2).

Researchers represented that prescribing sucrose can significantly reduce albumin levels 45 days after the continuous use of sucrose and the use of aspartame can also significantly decrease serum albumin levels (26). Other researchers also found that 10% of sucrose had no significant effect on serum albumin levels (27). The results of the study showed that the use of Cipla had no significant effect on serum albumin levels.

According to another study, the use of saccharin and aspartame had no significant effect on serum bilirubin levels (28). Using natural sweetener Oxime V, it was revealed that the amount of bilirubin increased in the serum (29). The results of studies using neotame indicated that the mentioned sweetener had no significant effect on the amount of bilirubin (30). The results of the present study demonstrated that the use of Cipla has no significant effect on serum bilirubin levels, which is in line with the findings of Shastry et al (14) in this regard.

Conclusions

Overall, the obtained results indicated that Cipla demonstrated no effect on the serum biochemical parameters and could be used without considering its effect on serum biochemical parameters.

Conflict of Interests

The authors declare that they have no conflict of interests.

Ethical Issues

In this research, ethical considerations have been fully observed.

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