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Research Article

THE EFFECTS OF LOW CALORIC COMMERICAL SWEETENER "*MARDIN* " AND SUGAR ON SERUM GLUCOSE AND LIPID PROFILELS IN RATS

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ABSTRACT
Sucralose is a non-nutritional artificial sweetener with a chemical formula $C_{12}H_{19}CL_3O_8$. Sucralose is the only non-caloric sweetener, which is derived from sugar or sucrose. Sucralose is sweeter than sugar 600 times and has high stability against heat. Mardin as a commercial sweetener in addition to sucralose has various compounds consisting lactose, L-Leucine, Cross, carmolase sodium and PVP also produces low rate calorie. Therefore, this research was conducted on the impact of Mardin on serum glucose and lipid profiles in rats. In this study, 18 male Wistar rats weighing about 220 ± 20g were divided into 3 groups each of which consisted of 6 rats. The groups were as follows: control group, sucralose and sugar group. Controls received no intervention. Sucralose group received Mardin (sucralose) with a Dose of 15 mg / kg daily for one month by gavage. Due to the amount of commercial sweetener tablets, which is equal to 2.7 grams of sugar, it was calculated for daily use of sugar group for one month by gavage. At the end of the period, blood sampling and serum separation was done; then, serum glucose and lipid profiles, including HDL, LDL, and total cholesterol and triglyceride measurements were conducted using diagnostic kits and spectrophotometric methods. The results were analyzed by SPSS (version 18.0) and a nonparametric Kruskal-Wallis test. The results revealed that there was no meaningful difference about understudied factors, so it can be concluded that Mardin has no adverse effect on understudied biochemical markers hence it is not prohibited for obese and diabetics.

Keywords: *Mardin, Sucralose, Lipid Profiles, Rat*

INTRODUCTION
Today, due to changes in the lifestyle of human societies, cardiovascular disease, obesity, diabetes and other metabolic disorders is expanding and that has caused human to turn after artificial sweeteners. Low-calorie sweeteners, has a sweet taste, with low or few calorie thus checking the body weight gain. Sucralose with chemical formula C12H19CL3O8 is the only no-calorie sweetener derived from sugar. Sucralose is 600 times sweeter and its taste is like sugar; and in addition, its resistance to pasteurization heat makes it superior. Therefore it is used as a sugar substitute in various foods, beverages, desserts, chewing gum, sauces, pharmaceutical products, and dietary supplements. Since oral bacteria do not know sucralose as a food source, so will not cause dental decay. According to the final report of the European Scientific Committee on Food, sucralose is broken down into 4-CG and 1,6 DCF as a result of hydrolysis. The small molecules are resistant to more hydrolysis and complete analysis due to sucrose chlorinated into sucralose that change molecule conformation and makes it resistant against glycoside enzymes in the digestive tract where it normally causes the breakdown of carbohydrates (SCF/CS/ADDS/EDUL/190 Final 2000). The acceptable daily intake (ADI) of Sucralose in the human being is 15mg/kg and according to pharmacokinetic studies, it has been demonstrated that over 85% of sucralose is excreted in the feces without absorption in the gastrointestinal tract and only 15% of the consumed sucralose is absorbed by the gastrointestinal tract as an inactive release (Ademir, 2009). In a study in which the impact

of 2-20 mg / kg sucralose was examined in rats revealed that 80% and 9-16 % of sucralose is excreted in urine and feces respectively, While sucralose reabsorption in the kidney tubules is a minimal amount and below 5% within 24 hours (Simes *et al.*, 2000). Sucralose metabolites are excreted from the body in two ways: a) restoring to the substances called 1.6 D chloro aminitol and excretion via urine flow and b) conjugation with glutathione (Ademir, 2009).

A study showed that people who use a lot of artificial sweetener receive more calories compared with others which ultimately intensify their obesity since artificial sweeteners destroy the natural mechanisms of appetite and the individual don't feel enough satiety so uses other foods largely. Mardin commercial tablets in addition to sucralose have various compounds like lactose, L-Leucine, Cross, carmolase sodium and PVP which also produce low rate calorie. Therefore, this research was conducted to see the impact of Mardin on serum glucose and lipid profiles in rats.

MATERIALS AND METHODS

In this study, 18 male Wistar rats weighing about 220 ± 20 g were divided into 3 groups each of which consisted of 6 rats. The groups were as follows: control group, sucralose and sugar group. Controls received no intervention. Sucralose group received Mardin (sucralose) with a Dose of 15 mg / kg daily for one month by gavage. Due to the amount of commercial sweetener tablets, which is equal to 2.7 grams of sugar, it was calculated for daily use of sugar group for one month by gavage. At the end of the period, blood sampling and serum separation was done; then, serum glucose and lipid profiles, including HDL, LDL, and total cholesterol and triglyceride measurements were conducted using diagnostic kits and spectrophotometric methods. The results were analyzed by SPSS (version 18.0) and a nonparametric Kruskal-Wallis test.

RESULTS AND DISCUSSION

Results

Glucose

According to Table (1) and using nonparametric Kruskal-Wallis test, the means of glucose in control, sugar treatment, and commercial sweetener groups were 111, 104, and 106 mg/dl, respectively, based on $X^2 = 0.293$ at significance level p = 0.864 and at the confidence level 95% the observed difference in the mean glucose level of the three groups was not significant (P>0.05).

Table 1: Comparison of the mean glucose level (mg/dl) by group separation

Group	Number	Mean	Variation range	X^2	P
Control	6	111	46		
Sugar	6	104	48		
Commercial sweetener	6	106	60		
Total	18			0.293	0.864

Cholesterol

According to Table (2), the mean of cholesterol in control, sugar treatment, and commercial sweetener groups were 56.50, 68.50, and 56.50 mg/dl, respectively, based on $X^2 = 4.328$ and at significance level p = 0.864 and at the confidence level 95% the observed difference in the mean cholesterol level of the three groups was not significant (P>0.05).

Table 2: Comparison of the mean cholesterol level (mg/dl) by group separation

Group	Number	Mean	Variation range	X^2	P
Control	6	56.50	36		
Sugar	6	68.50	18		
Commercial sweetener	6	56.50	33	4.328	0.115
Total	18				

Triglyceride

According to Table (3), the mean of Triglyceride in control, sugar treatment, and commercial sweetener groups were 148.50, 137.50, and 126 mg/dl, respectively, based on $X^2 = 0.272$ and significance level P = 0.873 and at the confidence level 95% the observed difference in the mean cholesterol level of the three groups was not significant (P>0.05).

Table 3: Comparison of the mean triglyceride level (mg/dl) by group separation

Group	Number	Mean	Variation range	X^2	P
Control	6	148.50	79		
Sugar	6	137.50	111	0.272	0.873
Commercial sweetener	6	126	149		
Total	18				

HDL

According to Table (4), the mean of HDL in control, sugar treatment, and commercial sweetener groups were 39, 49.50, and 37.5 mg/dl, respectively, based on $X^2 = 5.356$ and significance level P = 0.069 and at the confidence level 95% the observed difference in the mean HDL level of three groups was not significant (P >0.05).

Table 4: Comparison of the mean HDL level (mg/dl) by group separation

Group	Number	Mean	Variation range	X^2	P
Control	6	39	13		
Sugar	6	49.50	21	5.356	0.069
Commercial sweetener	6	37.50	25		
Total	18				

LDL

According to Table (5), the mean of LDL in control, sugar treatment, and commercial sweetener groups were 31, 39, and 55.50 mg/dl, respectively, based on $X^2 = 4.386$ and significance level P = 0.112 and at the confidence level 95% the observed difference in the mean LDL level of three groups was not significant (P >0.05).

Table 5: Comparison of the mean LDL level (mg/dl) by group separation

Group	Number	Mean	Variation range	X^2	P
Control	6	31	23		
Sugar	6	39	51		
Commercial sweetener	6	55.50	58	4.386	0.112
Total	18				

Discussion

In a study (Shastry *et al.*, 2012) that was conducted by oral administration of sucralose based on ADI dose equal to 15 mg / kg in three phases of 0-3 weeks of the 1 × ADI, 3 - 7 weeks of 2×ADI, and 7-13 weeks of 4× ADI, the decrease in serum glucose was reported in all phases only with the difference that the decrease was very minimal but in phases 2 and 3 the reduction was apparent but not meaningful which is similar to the results of the present study. In a study conducted by Mezitis (1996) it was demonstrated that sucralose with a dose of 1000 mg had an increasing effect on serum glucose which is similar to the results of the present study.

In another study conducted by Shastry *et al.*, (2012), the amounts of serum lipid profiles in phases 2 and 3 had a meaningful increase while in phase one oral administration of sucralose to the rats, according to ADI dosage was equal to 15 mg/kg has been conducted in a period of 0-3 weeks, the treatment group lipid

profile had not apparent change compared with a control group which is conformed to the results of the present study.

In a research conducted by Helen in 2013 in which the effect of sucralose-contained commercial tablet, Splenda, on healthy and diabetic rats was studied, it was revealed that sucralose decreased serum glucose level about 14% in healthy animals compared with a control group that didn't conform to the results of the present study in which a minimal and meaningless decrease of serum glucose was observed. Also in that study, increased levels of cholesterol, HDL, and LDL by 20, 25, 38 percent, respectively, and decreased level of triglyceride by 17% in sucralose group compared with the control group was reported that doesn't conform to the results of the present study. In that study, 25% reduction in insulin in the diabetic group, a 222 % increase in serum glucose, a 26 % increase in total cholesterol, 25% reduction in HDL, a 75 % increase in LDL, and 98% increase in triglycerides, have been reported. Furthermore, it was proved in the Research (Helen *et al.*, 2013) that there was a 150 % increase in glucose, 22% reduction in insulin, 46% increase in total cholesterol, 14% decrease in HDL, a 138 % increase in LDL and 56% increase in triglycerides in diabetic-sucralose group that conforms to the findings of this study in which there was approximately 5% reduction of serum glucose in normal rats fed sucralose. Mardin suppressive effect on serum glucose may be related to its decreased absorption in the gastrointestinal tract.

In vitro studies have shown that sucralose induces insulin secretion via mechanisms related to calcium and CAMP (Nakagava *et al.*, 2009). In the present study there was no change in sucralose group cholesterol compared with control group while in the study conducted by Mathe (1995); increased cholesterol has been reported following to the consumption of sucralose due to increased intestinal absorption or increased cholesterol synthesis.

In this study, serum triglycerides of sucralose group has decreased in comparison to the control group that isn't consistent with the results of CFS emenkovich's study (Emenkovich's *et al.*, 1989) in which increased triglyceride levels were reported after consumption of sucralose. In Ferre's study the decrease in triglycerides after consumption of sucralose has been confirmed whcih is consistent with the present results. This reduction may be due to the effect of sucralose on PPAR-α, which leads to the expression of lipoprotein lipase as well as activation of PPAR-У in adipose tissue and increased triglyceride levels (Ferre, 2004). In a study conducted by Fruchart *et al.*, (2001) increased level of HDL has been reported after the consumption of sucralose that is not consistent with the results of the present study in which meaningless increase and decrease of LAD and HDL has been reported. In general it has been seen that there is no meaningful changes in serum glucose and lipid profiles in sucralose group compared with control group. In addition, citing the results of the study conducted by Grotez *et al.*, (2003) in which it has been reported that sucralose consumption with the dose of 7.5 mg/kg had no effect on serum glucose of type 2 diabetes, it can be concluded that sweetener tablet, Mardin, has no side effect and contradiction for obesity and diabetes.

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