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Original Article

Relationship Between Artificial Sweeteners Intake With Diabetes in Experimental Rats

Norah Abdullah Mohammed Fahad Al-Hazzaa, Abdelrahman R Ahmed

Food and Nutrition Science Department, Agricultural Science and Food, King Faisal University, Al-Ahsa 31982, Saudi Arabia

Correspondence

Norah AMF Alhazzaa

Food and Nutrition Science Department, Agricultural Science and Food, King Faisal University, Al-Ahsa 31982, Saudi Arabia

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Abstract

The artificial sweeteners have been used in many food industries and young and adults' ones accept the taste of very sweet taste and low calories compared to natural sweeteners and became marketed on the basis that it is possible to control and reduce diabetes and the effects of these artificial sweeteners, But the manufacturers are unaware of the side effects that may be caused in the long term.

Methods: *The current research was carried out to know the effect of artificial sweeteners on low blood sugar in experimental rats. For this purpose, rats were divided to three groups with adding different artificial sweeteners (Aspartame, sucralose, saccharine) at the same dose level (10 gm/kg fed basal); the control group of rats was fed a basal diet without any sweeteners for 8 weeks.*

Results: *The feeding of rats on sucralose and aspartame led to a high significant with statistically significant increase in the level of Blood glucose (125±7 mg/dL, 123±10 mg/dL) compared to the control group, while the saccharin group was not affected by the blood glucose level after the 8 weeks study period.*

Conclusion: *It was concluded that artificial sweeteners had an effect on increasing blood glucose levels in male rats, and therefore they could not be included in the diets, especially for diabetic patients.*

Introduction

Diabetes is widespread around the world and is considered a risk factor that negatively impacts the health of individuals and society across all age groups. The American Diabetes Association suggested reducing this risk by using artificial sweeteners [1]. However, artificial sweeteners have been found to lead to glucose intolerance [2,3].

The American Diabetes Association recommended reducing the consumption of sugary sweetened drinks because of their dangerous connection to diabetes [4]. The number of diabetes patients worldwide increased from 108 million in 1980 to 422 million in 2014 [5]. The World Health Organization predicted that diabetes would be the seventh leading cause of death by 2030 [6]. In the United States, about 26.1 million people (9.3%) have diabetes [7].

In the Kingdom of Saudi Arabia, including regions such as Makkah, Madinah, Al Jawf, and the Eastern Region, the prevalence of diabetes is 30% [8].

Many studies agree on the effects of artificial sweeteners on increasing blood glucose. Mitsutomi et al. [9] studied the effect of artificial sweeteners on type 2 diabetes, obesity, and metabolism in rats. Fagherazzi et al. [10] followed a group of women to evaluate the relationship between the consumption of 100% fruit juice, sugar-sweetened beverages, artificial sugar-sweetened beverages, and the risk of type 2 diabetes. The results showed a correlation between both sugar consumption and artificial sugar consumption with an increased risk of type 2 diabetes, although there may be other uncontrolled factors responsible for this association with diabetes.

Bissonnette et al. [11] studied the effect of artificial sweeteners (saccharin and aspartame) added to a liquid diet on calorie volume and quantity in Western mice. The results showed that the group consuming aspartame had higher blood sugar levels compared to the other groups.

Materials and methods

Materials

Artificial sweeteners used in the study were sourced from reputable suppliers:

- Saccharin from Tamimi Markets Company
- Sucralose from Ahmad Yousof Almasnad Trading Corporation
- Aspartame from Green Wave Company

Blood sugar levels were analyzed using the Accu-Chek Instant glucose meter by Roche.

Experimental Diet

The experimental diet was prepared using ingredients sourced from the local market in Hufuf City, KSA. The composition of the diet per 100 grams included:

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65% corn, 15% wheat bran, 4.3% soya beans, 0.35% salts, 0.2% vitamins and minerals, 3.85% calcium carbonate, 0.8% mono calcium phosphate (MCP), 10% distiller dried grains (DDGS)

The sweetened substances (saccharin, sucralose, and aspartame) were added at a concentration of 10 grams per 100 grams of food [12]. The mixture was then formed into molds using eggs.

Experimental Animals

Thirty-two male mice weighing between 180-200 grams were obtained from the Veterinary Teaching Hospital at King Faisal University, Al-Ahsa, Kingdom of Saudi Arabia. Prior approval was obtained from the Animal Ethics Committee. The mice were housed in cages made of plastic and stainless steel, maintained at a temperature of 22°C with 50% humidity [13] in the animal house of the Veterinary Medicine Teaching Hospital.

Methods

Experimental Design

The mice were divided into four experimental groups, each consisting of 8 animals. The groups were as follows:

- Control group: fed a normal diet only.
- Experimental groups:
  - Group 2: fed on aspartame
  - Group 3: fed on saccharin
  - Group 4: fed on sucralose

Each experimental group received one gram of the respective sweetener per 100 grams of basal diet along with water for a duration of 8 weeks [13].

Measurements

Feed Intake: The net food intake of each rat was monitored weekly, accounting for any residual food left over, to assess the impact of the experimental diets [14].

Results and Discussion

Results are expressed as mean ± standard deviation (SD), n = 8. The blood glucose levels of tested rats (1, 2, and 3) received aspartame, sucralose, and saccharine at a concentration of 10 mg/kg each.

As shown in Table 1, the average consumption of regular basal and sugars added at a constant concentration was monitored throughout the experiment. There were statistically significant differences ($p \leq 0.05$) observed between the control group and the sucralose group. Additionally, the average basal consumption in the saccharin group significantly increased compared to the sucralose group in the second week.

No significant differences were observed between the control group and the three tested groups (aspartame, sucralose, and saccharin) in the third week at the significance level of $p \leq 0.05$. Similar results were observed in the fourth and sixth weeks.

By the end of the fifth week, a highly significant difference was found between the sucralose and saccharin groups. At the end of the seventh week, a statistically significant but lower difference ($p \leq 0.05$) was observed between the control group and the sucralose group.

The results of this study align with findings from Mathur et al. [15], concluding that sucralose and aspartame increase blood sugar levels, with aspartame also showing resistance to insulin and relative glucose intolerance [16]. Anbara et al. [17] additionally reported that aspartame affects protein metabolism and endocrine balance due to methanol oxidation to toxic formaldehyde. They also found that aspartame causes free radicals and oxidative stress, potentially damaging the male reproductive system, whereas saccharin did not affect blood sugar levels, contrasting with the findings of Leibowitz et al. [18], who observed an increase in blood glucose levels with saccharin use.

Conclusion

The current study indicates that artificial sweeteners may increase blood sugar levels over an 8-week period. It was concluded that both aspartame and sucralose led to a significant increase in blood glucose levels. Therefore, it is recommended that these artificial sweeteners should not be included in the diet, especially for diabetics, due to their association with numerous complications harmful to public health. Instead, natural sweeteners should be considered as alternatives.

Recommendation

This study recommended that future research to focus on knowing the effect of artificial sweeteners on tissues of fat and liver.

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Table 1. *Effect of artificial sweeteners on feed intake (gm/rat)*

Treatments	Week1	Week2	Week3	Week4	Week5	Week6	Week7	Week8
C	82±18a	117±24d	112±35a	140±34a	200±41c	152±12a	187±34d	157±21b
1	82±21a	65±9b	140±12a	140±12a	148±16b	140±14a	105±31b	148±27b
2	82±10a	48±11a	125±17a	164±33a	242±39d	160±56a	54±9a	69±25a
3	82±20a	85±16c	140±19a	140±22a	87±33a	146±42a	152±23c	137±44a

Values mean ± standard deviation (SD) (n = 10).

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