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The Effect of Acesulfame k and Aspartame as Sweetener Materials in Food Products on Body Parameters of Rats

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ABSTRACT

The objective of the current study is to highlight the effects of acesulfame k and aspartame as sweetener materials in food products on a variety of rat parameters. In this study determined insulin hormone,T3, T4, and testosterone hormone levels, glucose, urea, creatinine, and the lipid profile and the uric acid concentration in blood serum was determined. The results revealed that there was no significant change in insulin level, testosterone hormone, T3 hormones and T4 hormones in the group of acesulfame k, but a significant increase in the aspartame group when compared to the placebo group. In comparison to control rats, urea and creatinine levels increased significantly in the acesulfame k group and also significantly in the aspartame group. The current study found a significant decrease in acesulfame k and aspartame group animals compared to control animals. There was no significant difference between the acesulfame k and aspartame groups. The experiment clearly demonstrated that acesulfame k has lower effects than aspartame and that it is necessary to avoid the use of artificial sweeteners due to the numerous obvious and dangerous effects on hormones, lipid profile, protein profile, and multiple physiological parameters of the body.

Keywords: *Food additives, Artificial sweeteners, Acesulfame potassium, Aspartame, Physiological parameters*

INTRODUCTION

Food sweeteners are food additives that provide a sweet taste similar to sugar, but differ in that food energy is less than what is found in sugar. Processed sweeteners are typically created through the extraction of plants or through chemical synthesis1. Companies provide food sweeteners to customers to use in beverages for instance coffee, tea, and many hot drinks, or in various foodstuffs. They are put in paper containers that are colorful and small depending on the country and type of sweetener. Food sweeteners such as acesulfame potassium and aspartame are used in the diet because it is free of energy in addition to sweetening drinks2.

Acesulfame K is a high-density industrial plant food sweetener. It has a long shelf life and has good resistance to high temperatures. It is found in a variety of foods, such as baked goods, gum, canned goods, desserts, and drinks3. When the acesulfame k is used in high concentrations above normal levels, it may have an unpleasant aftertaste. It is very stable with normal food preparation and processing, and it is heat resistant, so it is suitable for cooking and baking. Some people believe that acesulfame k is safe to use because the body does not metabolize it and excretes it by the kidneys without changing it. Furthermore, numerous safety studies have been conducted, with no adverse effects reported4. The other most common type of sweetener is aspartame. It usually contains substances found in the human body and also in the diet (phenylalanine, amino acids, aspartic acid, and methane alcohol). Aspartame is rapidly and completely metabolized into its three components after ingestion by humans and experimental animals5. Aspartame consumption has been linked to neurological and behavioral problems in people who are sensitive to it. Headache, insomnia, and seizures are among the expected neurological side effects. Furthermore, the effects could include changes in regional brain concentrations of a monoamine neurotransmitter, specifically catecholamines6. Furthermore, increased aspartame consumption may be associated with the risk of the pathogenesis of some mental disorders, as well as some compromises in the learning process and emotional functioning7. By combining two essential phenylalanine and amino acids, aspartic acid is the most widely used sweetener of the new generation. It's worth noting that aspartame occurs naturally in the majority of protein-containing foods, including meats, dairy products, and some vegetables. Aspartame is broken down into phenylalanine, aspartic acid, and a trace of methanol after digestion8. Aspartame is used to enhance and intensify flavors, particularly citrus and fruits. It is also used to sweeten a wide range of foods and beverages. According to some studies, aspartame is safe and suitable for diabetics, pregnant women, and children9. In general, there are several factors that contribute to the risks of consuming food sweeteners in various types of food in many countries around the world, including Iraq. The most prominent of these factors is the lack of legal health legislation specifying the types of food sweeteners that are allowed or prohibited to use because they are harmful to health, the scarcity of specialized laboratories to examine the presence of food additives, the absence of a role for health institutions in implementing and activating the supervisory role and inspection of the presence of harmful substances such as artificial food additives in foodstuffs, particularly those imported and manufactured locally, the lack of coordination and continuous scientific health communication with international health institutions such as the FDA, which is in charge of determining the safety of food additives, as well as the indifference to implementing their recommendations and adhering to global health guidelines10. Because artificial sweeteners are increasingly being used in food products, it is critical to investigate the effects of these food additives on body parameters. The purpose of this study is to determine the effects of acesulfame k and aspartame as sweetener materials in food products on a variety of rat parameters such as hormones, protein profile, body weight, biochemical parameters, and lipid profile. In addition, by conducting tests on laboratory animals, it is possible to demonstrate the possibility of potential dangers as a result of the use of food sweeteners in the human body

METHOD

In this study, thirty-six male rats weighing 110 to 130 g were used. The animals were housed in stainless steel separate cages in the kut technical institute's animal house. The animals were divided into three equal groups of twelve rats each, as follows: The first group consisted of untreated rats, the second of rats given acesulfame k (15 mg/kg b.w. /day), and the third of animals given aspartame (50 mg/kg b.w. /day). The body weights of the experimental animals were measured at the start and end of the experiment. The animals were decapitated after 30 days to begin the laboratory tests. The blood samples were collected for the various analyses, and all blood samples were centrifuged for 15

minutes at 5000 rpm, and the supernatant was separated for analysis. In this study, thirty-six male rats weighing 110 to 130 g were used. The animals were housed in stainless steel separate cages in the kut technical institute's animal house. Rats were divided into three equally groups [untreated, treated with acesulfame k (15 mg/kg b.w./day), and treated with aspartame (50 mg/kg b.w./day)], each with twelve rats: At the beginning and end of the experiment, the body weights of rats were measured. After 30 days, the animals were beheaded to start the laboratory tests. The blood samples were collected for the various analyses, and the supernatant from each blood sample was cooled and centrifuged at 5000 rpm for fifteen minutes.

Biochemical Analysis

In this study determined insulin hormone using an ELISA kit in the current study's hormone analysis (10-1250-01, Mercodia AB, Uppsala, Sweden). A free online calculator was used to compute the HOMA-2 IR index. "(HOMA Calculator, Version 2.2.3, Diabetes Trail Unit, The University of Oxford, Oxford, UK)"

HOMA-IR= ([(Glycaemia (mg/dl)/18.2) ×Insulin (mU/ml)])/(22.517) 11

In addition, the T3, T4, and testosterone hormone levels were determined using an automated quantitative test "VIDAS® kits". BioMerieux SA kits, France, were used to test glucose, urea, creatinine, and the lipid profile, which included total cholesterol, triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL).

The uric acid concentration in blood serum was determined using the Spanish Spinreact kit. The Tietz method12 was used to calculate total bilirubin in blood serum. After estimating total protein and albumin concentrations, calculated the concentrations of serum globulin using the following formula: "Globulin (g/dl) equals total protein (g/dl) –albumin (g/dl)13.

Statistical Analysis

Data feeding was followed by descriptive and analytic statistics using SPSS version 21. The results were expressed as the Mean Standard Error of the Mean. The T-test was used to determine the significance of the difference in proportions between variables. Bonferroni's test was used to compare the significance of groups. The results were considered statistically significant when P = 5% to >1% denoted significant and =1% denoted highly significant statistical test results.

RESULTS

The current study was carried out at the Kut Technical Institute's animal house, and the examinations were carried out in specialized medical laboratories. The outcomes of 36 rats divided into three groups of rats (group of control, acesulfame k group and aspartame group).

In terms of insulin levels, the current study found that there was no significant change in the acesulfame k group, but there was a significant increase (p 0.05) in the aspartame group when compared to the control group. Concerning T3 and T4 hormones, there was no detectable change in the levels of both hormones in an acesulfame k group, but the aspartame group showed a significant decrease (p 0.05) in hormone concentrations when compared to the acesulfame group. (Table 1).

TABLE 1: The effect of acesulfame k and aspartame on hormones of treated animals.

Variables	Control groups	Acesulfame k	The change from control %	Aspartame	The change from control %
Insulin (mlU/ml)	0.94 ± 0.006	0.99 ± 0.008	8%	1.6 ± 0.039 *	37%
T3 (ng/dl)	46.8 ± 0.4	45 ± 1.1	-5%	40 ± 1.72*	-14%
T4 (µg/dl)	3.045 ± 0.007	2.9 ± 0.16	-6%	2.1 ± 0.41*	-37%
Testosterone (ng/dl)	1.05 ± 0.005	0.97 ± 0.04	-7%	0.49 ± 0.05*	-45%

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The statistical analysis of values demonstrates mean ± standard error

P* < 0.05 compared to control groups

In terms of body weight, there was no significant change in the acesulfame k group animals, but there was a highly significant increase (p 0.01) in the aspartame group compared to the control group. In terms of glucose levels, there was no significant change in the acesulfame k group animals, but there was a significant increase (p 0.05) in the aspartame group animals compared to the control group animals. In terms of renal function tests, urea and creatinine levels increased significantly (p 0.05) in the acesulfame k group and significantly (p 0.05) in the aspartame group compared to control rats. In terms of uric acid, the current study found a significant decrease (p 0.05) in acesulfame k and aspartame group animals compared to control animals. In terms of total bilirubin, the current study's findings revealed that there was no significant difference in total bilirubin between the acesulfame k and aspartame groups. (Table 2).

TABLE 2: The effect of acesulfame k and aspartame on body weight and biochemical parameters of treated animals.

Variables	Control groups	Acesulfame k	The change from control %	Aspartame	The change from control %
The body weight change %	7.9 ± 0.4	8.9 ± 0.5	9%	13 ± 0.8**	38%
Glucose (mg/dl)	107 ± 0.6	114 ± 1.4	4%	123 ± 0.7*	11%
Urea (mg/dl)	35.8 ± 0.59	44 ± 1.4*	15%	59 ± 0.7*	50%
Creatinine (mg/dl)	1.22 ± 0.032	1.4 ± 0.11*	34%	2.5 ± 0.08*	93%
Uric acid (mg/dl)	3.7 ± 0.05	2.6 ± 0.05*	-33%	2.5 ± 0.07*	-36%
Total bilirubin (mg/dL)	0.13 ± 0.03	0.08 ± 0.01	-27%	0.09 ± 0.02	-30%

The statistical analysis of values demonstrates mean ± standard error

P* < 0.05, P** < 0.01 compared to control groups

In terms of lipid profile, the current study found a significant increase (p 0.05) in cholesterol and triglyceride levels in the acesulfame k and aspartame groups, respectively, when compared to control animals. The HDL level decreased significantly (p 0.05) in the acesulfame k group, while the aspartame group experienced a highly significant decrease (p 0.01). In terms of LDL levels, the acesulfame k group showed no significant change, whereas the aspartame group showed a significant increase (p 0.05) in comparison to the control animals. In both the acesulfame k and aspartame groups, there was no significant difference in VLDL levels when compared to the control group. (Table3).

TABLE 3: The effect of acesulfame k and aspartame on lipid profile of treated animals.

Variables	Control groups	Acesulfame k	The change from control %	Aspartame	The change from control %
Triglyceride (mg/dl)	133 ± 0.6	141± 1.5*	4%	148 ± 0.8*	10%
Cholesterol (mg/dl)	123.4 ± 0.42	129 ± 1.8*	6%	142 ± 1.4*	18%
HDL (mg/dl)	60.3 ± 0.51	54 ± 1.3*	-8%	44 ± 0.6**	-25%
LDL (mg/dl)	33.9 ± 0.47	45 ± 2.8	29%	68 ± 2.3*	90%
VLDL (mg/dl)	28 ± 0.1	30 ± 0.7	5%	33 ± 1.5	12%

The statistical analysis of values demonstrates mean ± standard error

P* < 0.05, P** < 0.01 compared to control groups

In terms of protein profile, the current study found a significant decrease (p 0.05) in albumin levels in the acesulfame k and aspartame groups, respectively, compared to control rats, while there was no significant change in globulin levels in either group compared to control animals, but total protein showed a significant decrease (p 0.05) in the acesulfame k group and a highly significant decrease (p 0.01) in the aspartame group (Table 4).

TABLE 4: The effect of acesulfame k and aspartame on Albumin, Globulin and Total protein of treated animals.

Variables	Control groups	Acesulfame k	The change from control %	Aspartame	The change from control %
Albumin (g/dl)	3.45 ± 0.048	2.4 ± 0.21*	-20%	1.2 ± 0.17*	-74%
Globulin (g/dl)	3.6 ± 0.026	3.3 ± 0.07	-4%	2.7 ± 0.15	-12%
Total protein (g/dl)	6.66 ± 0.06	5.7 ± 0.4*	-15%	3.7 ± 0.2**	-45%

The statistical analysis of values demonstrates mean ± standard error

P* < 0.05, P** < 0.01 compared to control groups

DISCUSSION

In recent years, there has been an increase in consumer demand for low calorie products such as jams, candy, jellies, carbonated beverages, canned foods, and dairy products around the world. Sweeteners such as aspartame and acesulfame k are currently available on the market. The simplest way to reduce calories is to replace high caloric food products with sweetened ones; thus, there is a clear use of various food sweeteners to achieve this goal14. The main and important feature of various food sweeteners is their similarity in taste to sugar, so their use has increased in recent years all over the world, but the important question remains, is the use of food sweeteners safe and without health problems for the human body15, 16. There is an important fact, which is the existence of multiple reasons that lead to the use of harmful food sweeteners or even their prohibition globally in terms of type or percentage of addition to foodstuff, as well as the tendency of some countries to import food products at lower prices because they are prohibited in healthy developed countries, so preventive health measures must be taken at the country level, which includes enacting health laws and legislation with strict hedging requirements17. Aspartame significantly increased insulin levels in the current study, which could be attributed to phenylalanine, a component of aspartame. Phenylalanine is an amino acid that is thought to be a nutrient signaling molecule that acts as a stimulating factor for the production of insulin18. The study also found that laboratory animals given aspartame had significantly lower levels of T3 and T4 hormones. Aspartame is made up of two amino acids, phenylalanine and aspartame, that are linked to methanol19. Aspartame's metabolism in the human body is further converted and metabolized to formaldehyde20. Another study on male albino rats found that formaldehyde causes the follicular epithelial cells of the thyroid gland to degrade, resulting in lower levels of T3 and T4 hormones. Another interpretation is that formaldehyde causes increased stimulation of thyroid follicles, which reduces the gland's synthetic capacity and may eventually lead to thyroid gland defect and failure21, 22. In the current study, there was a highly significant decrease in testosterone levels in laboratory animals given aspartame versus control animals. Aspartame reduces androgen hormone levels, which has an indirect effect on pituitary gland function23. Because of its importance in the regulation of aggressiveness in

mammals, it is widely accepted that testosterone deficiency causes negative social behavioral changes24. In this study, the aspartame animals had higher body weights than the control group, which could be attributed to aspartame increasing appetite via metabolites via various mechanisms25. Aspartame can significantly reduce leptin concentrations in the blood. Leptin is a hormone that is released by fat cells in adipose tissues and sends signals to the hypothalamus in the brain. This hormone aids in the regulation and modification of the body's long-term food intake and energy expenditure26. Leptin acts on the brain by inhibiting food intake, but low levels of leptin hormone can stimulate appetite, resulting in increased food intake27. Another study found that aspartame caused an increase in body weight and fluid intake in a group of rats28. In terms of glucose levels, the current study found that rats given aspartame had significantly higher glucose levels than the control group. The hyperglycemia in the aspartame group may be attributed to the formation of amino acids from aspartame, with phenylalanine being both glucokinetic and ketone, and aspartic acid being a partial amino acid (gluogin) and thus transformed to glucose29. The current study found a significant increase in urea and creatinine levels in rats given acesulfame k. In addition, rats given aspartame had significantly higher urea and creatinine levels. The elevated levels of urea and creatinine may be attributed to a defect in renal tissue permeability, tissue damage, and necrosis caused by the formation of free radicals in tissues as a result of glucose auto-oxidation and protein glycosylation30. Concerning the elevation of urea and creatinine in rats given aspartame, this could be due to a problem with glomerular filtration rate (a decrease in the glomerular filtration process) caused by the high level of methanol, which is a risk component of aspartame, causing abnormalities in the function and metabolism of multiple intracellular membranes of kidney cells31. In terms of lipid profile, the results of the experiment revealed that TG, TC, and LDL levels were significantly increased while HDL levels were significantly decreased in rats given acesulfame k and significantly increased in rats given aspartame when compared to the control group. Based on these findings, it is possible to conclude that the use of artificial food sweeteners may contribute to atherosclerosis. Furthermore, chronic aspartame use may cause and result in many changes in the lipid metabolism process, leading to hypercholesterolemia and atherosclerosis32-34. In the current study, there was a significant decrease in protein profile in both the acesulfame k and aspartame animal groups when compared to the control animals. There was a significant decrease in albumin and a highly significant decrease in total protein, which could be attributed to the inhibition effect of some food sweeteners on protein synthesis, which could lead to liver function failure. Furthermore, the lower protein profile in the treated groups may be due to hepatotoxicity and liver cell damage, which cause liver weakness and inability to produce proteins correctly and in accordance with actual need35,36.

CONCLUSION

The study confirmed and demonstrated that food sweeteners such as aspartame and acesulfame k should be avoided by consumers and food industries due to the risk effect on studying parameters.

The results of an experiment clearly showed that acesulfame k has fewer side effects than aspartame.

It is essential to avoid the use of artificial sweeteners due to the numerous obvious and dangerous effects on hormones, lipid profile, protein profile, and multiple physiological parameters of the body.

The use of natural sweeteners, with consideration for diabetics, as well as the use of very safe artificial sweeteners in extreme cases.

Abbreviations

T3: Triiodothyronine; T4: Thyroxine; FDA: Food and Drug Administration; ELISA: Enzyme-linked immunoassay; UK; United Kingdom; HDL:High-density lipoprotein; LDL:Low-density lipoprotein; SPSS: Statistical

Package for the Social Sciences; TC: Total cholesterol; TG = triglyceride.

Ethics Approval and Consent to Participate

The Ethics Committee of the Community Health Techniques department, Kut Technical Institute, Middle Technical University, Baghdad, IRAQ, granted ethical approval for the current study.

Competing Interest

The authors state that they have no competing interest.

Availability of Data and Materials

The corresponding author will make the resulting dataset available upon reasonable request.

Authors' Contribution

Each author made an equal contribution.

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