Effect OF Aspartame On Different Organs In Albino Rats And Comparing it With Some Other of Sugar Substitutes

Introduction

Sugar substitutes are compounds with many times the sweetness of sugar. As a result, much less sweetener is required and energy contribution is often negligible[1].

Natural sugar substitute as herbs (stevia), agave nectar,date sugar and fruit juice concentrate.[2].

Artificial sweeteners including aspartame, sucralose, acesulfame potassium and saccharin [1].

Use of Sugar Substitutes:to assist in weight loss, dental care, reactive hypoglycemia, diabetes mellitus[4].

Possible health concerns with sweeteners: artificial sweeteners maycause a variety of health problems, including cancer, hypoglycemia, orhyperinsulinemia and increased food intake the next time there is a meal (obesity) [2].

Natural sweeteners are generally safe, but they can lead to health problems such as tooth decay, poor nutrition, weight gain and increased triglycerides[9].

Aspartame is an artificial, non-saccharide sweetener. Aspartame is also one of the main sugar substitutes used by people with diabetes under the trade name Equal, Natra sweet and Canderel. FDA has set its ADI at50mg/kg[10]. Residual components of aspartame: Phenylalanine,aspartate andmethanol [5].

Stevia is a natural sugar substitute made from the leaves of the plant species Stevia rebaudiana. ADI is 4 mg/kg body weight.Stevioside is broken down into glucose and steviol[7].

Subjects and Method

We studied toxic effects of aspartame and stevia on albino rats. After 15 days of observation. Samples of aspartame, stevia were administered once daily subcutaneously for 2 weeks.

At the end of experimental period, the rats were anesthetized by ether inhalation and blood samples were obtained from all rat groups. Then samples of blood were collected. The heparinized blood was freshly used for blood count assay (hemoglobin, RBCS count,hematocrit and WBCs).Immediately after blood collection, the animals were dissected and tissues samples (liver) were got out from all rats within the different treatment groups.

Statistical analysis

All the data were expressed as mean ± standard error (SE) and P-value values of $P>0.05$ were considered no significantly

different, while those of P<0.05 and P<0.01 were considered significantly and highly significantly different, respectively

Result

The results revealed significant reduction in bodyweight gain (P<0.05) in aspartame and steviagroups andnon-significantreduction (P>0.05) in sucralose groups.

Table (1): Effect of aspartame, sucralose and stevia groups on body weight gain percent in different rat groups.

*

Experimental groups	**Body weight gain**		
Control group	30.63 ±2.4		
Doses given S.C	**0.625 mg/kg**	**1.875mg/kg**	**5.625mg/kg**
Aspartame groups	27.22±1.81*	25.47±1.87*	24.27±2*
Stevia groups	27.25 ±1.78*	25.14±1.6*	24.15±2.1*

Aspartame showed significant in dose 0.625 mg/kg reduction in hemoglobin, RBCs count and hematocrit and highly significant reduction in (1.875 and 5.625 mg/kg).Rats supplemented with stevia showed nonsignificant reduction in hemoglobin, RBCs count and hematocrit in all doses**.**

Rats supplemented with 1.875 mg/kg and 5.625 mg/kg aspartame exhibited significant reduction in WBCs count. While there were insignificant changes in WBCs in 0.625 mg aspartame group and all stevia groups.

Table (2): Effect of aspartame and stevia groups on hemoglobin (Hb) in different rat groups

Experimental groups	**HB**

	g/dl		
Control group	14.74±.9		
Dose given SC	**0.625mg/kg**	**1.875mg/kg**	**5.625mg/kg**
Aspartame groups	13. 81±0.8 *	13.05±0.73**	11.61±0.56**
Stevia groups	14.74±0.11 NS	14.68±0.1 NS	14.56±0.17 NS

Table (3): **Effect of aspartame and stevia groups on red blood cells count in different rat groups.**

Experimental groups	**RBCs (x 10 ^{6}/mm3)**		
Control group	7.6±0.6		
Doses given SC	**0.625mg/kg**	**1.875mg/kg**	**5.625mg/kg**
Aspartame groups	7.23±0.38*	6.75±0.6**	5.79±0. 35**
Stevia groups	**7**.44±0.6 NS	7.35±0.48 NS	**7**.52±0.54 NS

Table (4): Effect of aspartame, sucralose and stevia groups on hematocrit in different rat groups.

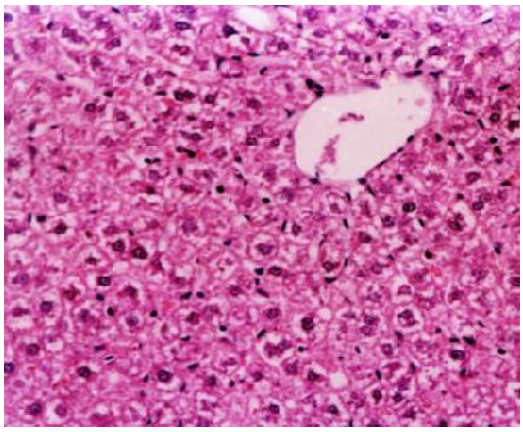
Experimental groups	Hct(%)		
Control group	38.35±0.7		
Doses given S.c	0.625mg/kg	1.875mg/kg	5.625mg/kg
Aspartame groups	37.47±0.6*	36.44±0.8**	35.47±0.64**
Stevia groups	38.32±0.29 NS	38.3±0.27 NS	37.9±1.11 NS

Table (5)Effect of aspartame, sucralose and stevia groups on white blood cells count in different rat groups.

Experimental groups	WBCs(x103/mm3)		
Control group group(A)	7.64±0.48		
Doses given s.c	0.625 mg/kg	1.875mg/kg	5.625mg/kg
Aspartame groups	7.39±0.54 NS	6.9±0. 24NS	6.71±0.72*
Sucralose groups	7.3±0.35 NS	7.27±0.44 NS	7.25±3 NS
Stevia groups	7.43±0.44 NS	7.43±0.59 NS	7.35±0.46 NS

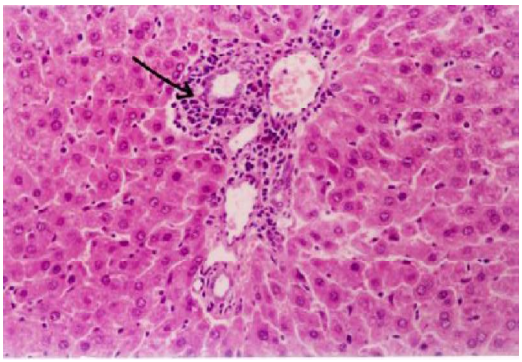
Pathological effect of aspartame and stevia groups on liver in different rat groups

The present study revealed that administration of aspartame induced hepatic cellular changes. As slight hydropic degeneration of hepatocytes in liver of rats administered Aspartame (0.625 mg/kg and 1.875 mg/kg).



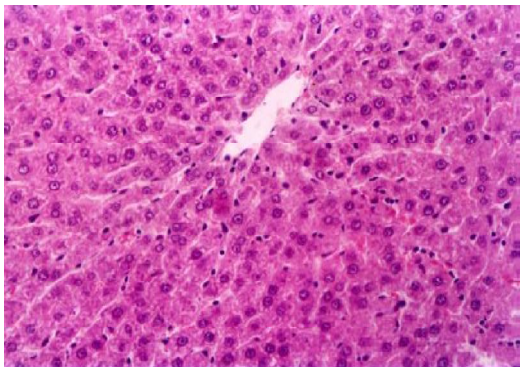
Microscopical examination of liver of rats administered aspartame(0.625 and 1.875 mg/kg) showed slight hydropic degeneration of hepatocytes.

Rats supplemented with aspartame 5.625 mg /kg showed portal infiltration with mononuclear inflammatory cells mainly lymphocytes and macrophagesin liver.



Liver of rats administered aspartame (5.625 mg/kg) showed portal infiltration with mononuclear inflammatory cells.

Stevia groups showed no hepatic cellular changes



Liver of rats administered stevia showing the normal histological structure of hepatic lobule from central vein and hepatocytes

Discussion

The present results showed significant reduction in body weight gain in aspartame groupsand stevia groups when compared to the control group.

In agreement with this result **Rolls(2000)** reported that both short term and long term studies have shown that consumption of aspartame sweetened foods or drinks is associated with a reduction in food intake. **Blundell and Hill** concluded that aspartame may lead to a loss of appetite. Most studies indicate that aspartame reduces food intake and may assist with weight control [(4)]

In disagreement, a 2005 study by Sharon Fowler of the University of Texas linked diet drinks to obesity, and we know that aspartame makes crave carbohydrates so gain weight. [13]

Stevia has been found to increase insulin sensitivity in rodent models and to have beneficial effects on blood glucose and insulin levels in human studies specially diabetic patients, which suggests it may have a role in food intake regulation[5]

In this study we found that aspartame induced highly significant reduction in Hb concentration, Hct% and RBCs count in rats took 1.875 mg/kg and 5.625 mg/kg aspartame and significant reduction in rats took 0.625 mg/kg of aspartame. WBC count are significant reduced count in rats which treated with 1.875 mg/kg and 5.625 mg/kg aspartame and non-significant changes in WBC in induced by 0.625mg/kg aspartame.

In agreement with **Dr. James Bowen (2002)** who wrote that aspartame cause mysterious breakdown of blood cells, and resultant anemia, was called "Lupus Erythematosis", the red wolf of the blood, which was supposedly devouring the red blood cells and causing anemia. Lupus Erythematosis is now often caused by aspartame, which triggers the immune system into an autoimmune status by altering the body's proteins with formaldehyde, which denatures them, and by damaging the body's genes with formaldehyde and formic acid[8].

In disagreement with **Leon, *et al*,2000.**Who evaluated the safety of administration of aspartame in a dose of 75 mg/kg/day in male and female volunteers for a period of 24 weeks. They found no significant changes in complete

blood cell count that included white blood cells that were reported within the normal ranges[6]

In this experiment, Stevia induced non- significant reduction in Hb concentration, Hct% and RBCs count in all stevia groups of rats and insignificant changes in WBC when compared to control rats.

By Dr. K. Toyoda and colleagues, from the Division of Pathology, For a period of 104 weeks (two years), three groups of lab rats 50 males and 50 females- were tested. One group received stevioside in a concentration that constituted 2.5 percent of its daily diet; the second group received a concentration that constituted 5 percent of its diet. The third group, which served as the control, received no stevoiside[13]

.As a result of this protracted and extensive investigation, it was concluded that no significant dose-related changes were found in the growth, general appearance, hematological and blood biochemical findings, organ weights, and macroscopic or microscopic observations, as a result of feeding male and female with Stevia extracts at levels up to 1% of their feed for about two years[7]

The present study revealed that administration of aspartame induced hepatic cellular changes. This is proved by slight hydropic degeneration of hepatocytes in liver of rats administered Aspartame(0.625 and 1.875mg/kg) and portal infiltration with mononuclear inflammatory cells mainly lymphocytes and macrophagesin liver ofrats administered Aspartame(5.625 mg/kg)

These results were in agreement with **Kamal *et al.* (2000)** who

noted that the activities of AST and ALP increased significantly after administration of aspartame to healthy adult albino rats for 5 weeks. The elevation in serum aminotransferase activities could be due to drastic physiological effects caused by free radicals interaction with cellular membranes or may be related to breakdown of liver parenchyma [11]

The administration of labelled aspartame to agroup of cirrhotic rats resulted in comparable label retention by tissue components, which suggests that liver function (or its defect) has little effect of formaldehyde formation from aspartame and binding to biological components. The chronic treatment of a series of rats with 200 mg/kg of non-labelled aspartame during 10 days resulted in the accumulation of even more label when given the radioactive bolus, suggesting that the amount of formaldehyde adducts coming from aspartame in tissue proteins and nucleic acids mmay be cumulative. It is concluded that aspartame consumption may constitute a hazard because of its contribution to the formation of formaldehyde adducts[12] Stevia showed no hepatic cellular changes.

This is agreement with studies have found the effect of hepatic cellular changes to be so low as to be insignificant as any steviol that passes through the intestinal tract is metabolized to steviol glucuronide and excreted in the urine. In fact, some studies have shown that stevia may actually be cancer preventive[11]

In disagreement with study found that although stevioside was not cancer causing, steviol, a metabolite of stevioside, is indeed mutagenic in the presence of a

specific metabolic activation system [3]

Summary and conclusion

This study revealed that administration of aspartame induced significant reduction in hemoglobin, RBCs count and hematocrit in all doses and significant reduction in WBCs count in large dose, hepatic cellular changes but Stevia is generally save.

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