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A HISTOMORPHOMETRIC EVALUATION OF EFFECTS OF SUCRALOSE INGESTION ON LIVER OF ALBINO RATS

Anatomy

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ABSTRACT

Sucralose is a non-nutritive sweetener used in a broad range of foods and beverages. The aim of the study was to demonstrate any histomorphometric changes in liver after sucralose ingestion. A dose of 3g/kg/day of sucralose dissolved in distilled water were given for 30 days to experimental rats by oral gavage whereas Control rats received equal quantity of distilled water. Liver Pieces each having thickness 5mm were taken for paraffin sectioning. 80 slides of 5 micron thick tissue sections were made from each liver and stained with Hematoxylin and Eosin (H & E) which were subsequently evaluated for histomorphometric changes. No significant change in the size of hepatocytes and size of nuclei of hepatocytes were observed between slides of control and sucralose treated rat livers. Sinusoidal width was found to be significantly increased in experimental rat livers as compared to control which is indicative of hepatic damage. A food additive so commonly used as sucralose deserves further investigations.

KEYWORDS

Sucralose, Artificial Sweetener, Histomorphometry. Sugar free

INTRODUCTION

In the modern world people have become aware of the fact that sugar is one of the commonest culprits for increase in weight and blood sugar in diabetes. As a result, large number of artificial sweeteners entered ino the arena of food market. The latest and the most popular is sucralose which is freely available over the counter. Sucralose is 600 times sweeter than sugar[1], does not cause dental caries[2], is safe for consumption in diabetes[3] and does not affect insulin level[4].

Sucralose after metabolism is absorbed in liver, kidney and GIT. Since liver is the detoxification organ of the body and most of the sucralose gets concentrated in the liver, it can damage the hepatocytes and destroy them. It is broken down into smaller amounts of 1, 6-dichlorofructose[5]. It is postulated that such chlorocarbon can cause interference in the metabolism and damage to organs of the body.

Some adverse effects have been reported in rats when consumption ranged between 1.1-11 mg/kg/day[6]. These adverse effects were reduction in the amount of good bacteria in intestines of rats by 50%, increase in pH level in the intestines, increase in body weight and levels of p-glycoprotein[6]. Its ingestion has also been found to cause shrinkage of thymus[7] and calcification of the kidneys[8].

The present research was aimed at bringing the objective results about effects of sucralose on liver, if any. Controversial feedbacks about the toxic effects of so commonly used a sweetener as sucralose has prompted the present study on histomorphometric changes in the liver.

METHODS

Inbred adult Wistar albino rats weighing about 150-200 g of either sex, were procured from animal house of University College of Medical Sciences,Delhi.

Care of animals was taken as per CPCSEA guidelines for care of animals. The animals were kept in separate cages in normal lighting conditions. They were fed food and water ad libitum. Group 2 consisting of 6 experimental rats was given sucralose orally by gavage in the dose of 3g/kg/day dissolved in distilled water for 30 days. Group 1 consisting of 6 control rats received equal quantity of distilled water.

The animals anesthetized with anesthetic ether were perfused with 10% formal saline. The liver was dissected out. Pieces each having thickness 5mm were taken for paraffin sectioning. 5 micron thick sections were cut using a rotary microtome. 80 slides per rat i.e 480 control rat liver slides and 480 experimental rat liver slides stained with H & E stain were used for histomorphometry. Pro express analyzer software was used to measure the linear distances. The data obtained was tabulated and subsequently analyzed by SPSS software version 17 using nonparametric Mann Whitney U Test.

Following variables were compared:-

1. Short diameter of nucleus of hepatocyte.
2. Long diameter of nucleus of hepatocyte.
3. Short diameter of hepatocyte.
4. Long diameter of hepatocyte.
5. Sinusoidal width.

RESULTS

Size of the nucleus of hepatocytes: Mean short and long diameters of nuclei in control rats were recorded as 5.63 ± 0.30 and 6.14 ± 0.32 microns respectively. Mean short and long diameters of nuclei in experimental rats were recorded as 5.26 ± 0.48 and 5.94 ± 0.27 microns respectively. Mean values of diameters of nuclei of hepatocytes in control and experimental groups have been tabulated in table 1 and 2 respectively. These mean values of various experimental groups were correlated with those of control groups using Mann Whitney U test. No significant change was observed when values of short and long diameter of nucleus in control were compared with experiments, p value being 0.109 and 0.200 for comparisons of short and long diameters respectively.

Table 1: Mean values of size of the nuclei (Short diameter and long diameter), size of the hepatocyte (Short diameter and long diameter) and sinusoidal width in control groups in microns.

Groups	Size of the nuclei (Mean±SD)		Size of the hepatocyte (Mean±SD)		Sinusoidal width (Mean±SD)
	Short D.	Long D.	Short D.	Long D.	
Control 1	5.40 ± 0.67	6.11 ± 0.57	13.71 ± 3.11	16.13 ± 2.93	7.34 ± 3.76
Control 2	5.50 ± 0.48	5.78 ± 0.53	13.87 ± 1.48	16.26 ± 2.07	7.11 ± 1.68
Control 3	5.22 ± 0.60	5.72 ± 0.60	14.61 ± 1.64	15.40 ± 1.38	6.65 ± 1.87
Control 4	5.99 ± 1.00	6.46 ± 0.97	15.25 ± 2.70	16.21 ± 2.44	6.85 ± 1.59
Control 5	5.85 ± 0.61	6.41 ± 0.67	15.08 ± 1.99	16.13 ± 1.12	7.02 ± 1.88
Control 6	5.86 ± 0.63	6.39 ± 0.86	15.23 ± 2.25	16.86 ± 1.58	6.24 ± 2.38

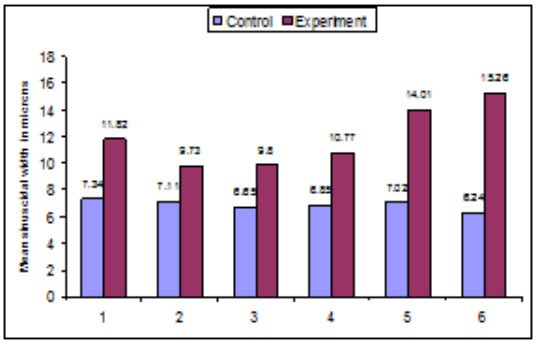
Table 2: Mean values of size of the nuclei (Short diameter and long diameter), size of the hepatocyte (Short diameter and long diameter) and sinusoidal width in experimental groups in microns.

Groups	Size of the nuclei (Mean±SD)		Size of the hepatocyte (Mean±SD)		Sinusoidal width (Mean±SD)
	Short D.	Long D.	Short D.	Long D.	
Experiment 1	5.80 ± 0.79	6.28 ± 0.81	14.20 ± 1.83	15.60 ± 1.35	11.82 ± 3.92
Experiment 2	5.24 ± 0.59	5.96 ± 0.55	15.61 ± 2.14	17.02 ± 1.41	9.73 ± 3.55
Experiment 3	5.28 ± 0.63	5.84 ± 0.89	14.37 ± 1.70	16.24 ± 1.33	9.80 ± 4.06
Experiment 4	5.10 ± 0.47	5.71 ± 0.66	13.96 ± 1.82	15.05 ± 1.84	10.77 ± 3.49
Experiment 5	5.72 ± 0.99	6.25 ± 0.80	14.73 ± 1.09	16.30 ± 2.01	14.01 ± 2.01
Experiment 6	4.44 ± 0.40	5.60 ± 0.56	14.45 ± 0.52	15.97 ± 0.66	15.26 ± 1.31

Size of the hepatocytes: Mean short and long diameter of hepatocytes in control rats were recorded as 14.62 ± 0.69 and 16.16 ± 0.46 microns. Mean short and long diameter of hepatocytes in experimental rats were recorded as 14.55 ± 0.57 and 16.03 ± 0.67 microns. Mean diameters of hepatocytes in control and experimental groups have been tabulated in table 1 and 2 respectively. These mean values of various experimental groups were correlated with those of control groups using Mann Whitney U test. No significant change was observed when values of short and long diameter of nucleus in control were compared with experiments, p value being 0.873 each for comparisons of short and long diameters.

Sinusoidal width: Mean sinusoidal width of control and experimental groups are tabulated in table 1 and 2 respectively. Mean sinusoidal width in controls were observed as 6.86 ± 0.38 microns whereas in experimental rats were found to be 11.89 ± 2.28 microns. Significant increase in the sinusoidal width in experimental groups as compared to control group was observed using Mann Whitney U test with p value 0.004 as shown in graph 1.

Graph 1: Sinusoidal width in control and experimental groups



DISCUSSION AND CONCLUSION

No significant change in the size of the hepatocytes was noted in the present study, indicating no effect of sucralose on the cellular activity. An increase in the hepatocyte area in diabetic rats has been reported[9] whereas a decrease in the volume of hepatocytes and their nuclei in streptozotocin induced diabetes in albino rats[10] has been observed. No alteration in the size of hepatocytes in our study reveals no effect of sucralose on glycemic response. This conclusion is consistent with the works suggesting lack of effect of sucralose in glycemic response in normal and diabetic individuals[3,11,12]. In the present study, sinusoidal width showed a significant increase in experimental rats as compared to controls. The effect of sucralose on the sinusoids has not been documented in the literature. However, sinusoidal dilatation in liver has been reported in tumour or granuloma formation[13], HIV infection[14], Rhuematoid arthritis[15], after administration of carbary[16] and monosodium glutamate[17]. These authors attributed this change to the toxic effect of drug/infection on the hepatocyte leading to shrinkage of the hepatocytes. On the available literature, sinusoidal dilatation seen in the present study can be implicated to deleterious effect of sucralose on hepatocytes. Sucralose which is increasingly becoming a routine food additive among every group of people in the society deserves extensive investigations on its effects on various organs, especially liver.

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