Aspartame Induced Hepatotoxicity in Male Albino Rats

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Abstract

Some dietary constituents can induce toxicity & play a critical role in the development of several hepatic disorders. Aspartame is widely used in many low-calories, non-weight bearing dietary alternatives, particularly in strategies of physical fitness and health. Thus, the present study investigated Aspartame Induced hepatotoxicity in male albino rats. Hepatotoxicity in rats treated with a blend of aspartame, which was studied by assessing parameters such as serum total protein, serum total lipid & serum liver enzymes. It was observed that serum total protein and serum total lipid were significantly increases serum liver transaminases in rats whose diets were supplemented with aspartame. Histopathological studies showed liver necrosis. The present study concludes that consumption of aspartame in diet induces liver tissue damage. Furthermore, the consumed doses of aspartame were mostly attributed to hepatocellular damage.

Keywords - Aspartame, Albino rats, Serum liver Enzymes, Hepatotoxicity

Introduction

Food additives are the substances which are not generally found in foods but are added in food products in order to improve its flavour, colour and sweetness. Additives include antioxidants, preservation, sweeteners, colorants, flavors, emulsifiers and stabilizers [1]. Sweeteners could be classified as natural nutritive and artificial non-nutritive sweeteners. Non-nutritive sweeteners are referred as intense sweeteners, extremely low caloric or alternative sweeteners. These were discovered in the last century, beginning with saccharin which was discovered in 1879 later, which was followed by many other artificial sweeteners including sucralose, cyclamate, acesulfame-k and aspartame [2]. There are various reasons of application of sweeteners in food. Earlier there was a medical need for developing artificial sweeteners, but nowadays people increasingly choose low-calorie product to reduce their calorie intake. Aspartame is one of the most widely used sweetener, discovered in 1965, produced commercially from the methyl ester of two amino acids, L-aspartic and L-phenyl alanine [3]. Aspartame was approved by the food and drug administration (FDA) in 1981. Aspartame is used mostly in foods that don't require cooking such as puddings, gelatins frozen desserts, yogurt, toppings and fillings in precooked bakery goods and cookies and carbonated soft drinks, instant tea and coffee, chewing gum and as a substitute for granulated sugar. The accepted daily intake recommended by FDA is 50 mg/kg b.wt/ day [4]. Clinically chronic exposure to aspartame was reported
to cause headache, brain tumors, insomnia, memory loss, nausea, slurred speech, personality changes, hyper activity and hearing problems [5]. The aim of this work was to study the histological and biochemical changes induced by long term intake of a recently used commercial sweetener i.e. Aspartame, to evaluate their hazardous effect on male albino rats.

**Experimental Materials and Methods**

Adult Swiss Albino rats weighing 180-200 gm were used in the present study, in which animals were maintained under normal condition and fed on a normal diet with free access to water ad libitum. Rats were randomly divided into four groups of 10 rats each.

**Group1**- The animals of this group were healthy normal rats and serves as untreated control groups.

**Group 2 to 3** - The animals of these groups were given blend of aspartame at a dose of 35 mg/kg and 70 mg/kg body weight/day. The blend as prepared by mixing aspartame in equal ratio, orally administered to experimental animals.

The animals were sacrificed after 90 days. The liver were quickly excised and fixed in Bouin's fluid for histological observation. 5 micro thick sections were prepared and stained by hematoxylin and eosin. Biochemical investigations were carried out on liver and serum collected from the experimental animals.

**Result**

Various Biochemical values from control and treated male rats fed with different concentrate of Aspartame which has been summarized in Table no.1 which depicted the following facts:

<table>
<thead>
<tr>
<th>S. No</th>
<th>Serum Biochemical Parameters</th>
<th>Control</th>
<th>Treatment (mg/kg b.wt)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>7 mg</td>
<td>35 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>‘T’ test</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>‘T’ test</td>
</tr>
<tr>
<td>1</td>
<td>Alkaline Phosphatase</td>
<td>134±20.45</td>
<td>0.4881</td>
</tr>
<tr>
<td></td>
<td></td>
<td>124±1.19</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>SGPT</td>
<td>32.7±8.53</td>
<td>2.2948*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>51.9±1.98</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>SGOT</td>
<td>143±21.95</td>
<td>1.6238*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>179.14±3.68</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Total Protein</td>
<td>214.85±2.47</td>
<td>1.4093</td>
</tr>
<tr>
<td></td>
<td></td>
<td>208.8±3.51</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Bilirubin</td>
<td>0.8±0.05</td>
<td>0.5570**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.83±0.02</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Glycogen</td>
<td>5.19±0.55</td>
<td>0.3270**</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5.01±0.02</td>
<td></td>
</tr>
</tbody>
</table>

*Almost Significant at P < 0.05; **Significant at P < 0.01; ***Non-Significant at P > 0.05
Table 1: Effects of Aspartame on Biochemical parameters in Albino rats after exposure of 90 days

It was observed that ingestion of Aspartame significantly increased total lipid, SGPT, SGOT and alkaline phosphate while total protein and glycogen significantly decreased as compare with control rat. The liver expressed extreme histopathological changes than the earlier dose. Microscopically, periportal necrosis was observed in the rats with yellow brown coloration. The hepatocytes were hypertrophied accompanied at some places by extensive proliferation of the bile duct epithelium leading to biliary obstruction. The centro-lobular and mid-zonal necrosis accompanied with hepatocytes, hypertrophy and hepatocytes hyperplasia was observed. Many fold enhancements was observed in number of swollen cells with nuclear degenerative changes. Binucleate condition was also observed in few hepatocytes.
Discussion

In the present study, preferably possible hepatotoxic effects of Aspartame in male Wister Albino rats have been assessed. The animals were intoxicated by sub-chronic treatment and various parameters were observed to analyze the effects of Aspartame. Following major tests were undertaken to evaluate the experimental hepatic injury in laboratory animals:

(i) Histological analysis of liver injury
(ii) Alteration in chemical constituents of liver and 3 Serum enzyme tests

Histopathological Analysis

Central vein and sinusoids show lymphocytic infiltration which is caused by toxics and normal inflammation reaction. Lymphocytes possibly secrete neutralizing and lytic enzymes which may be effective in detoxification of the toxic metabolites of food additives. Similar centrilobular necrosis was observed by feeding BHT in rats [6], and by feeding azo dyes to rats and mice [7,8]. The liver function tests performed in the present study are diagnostic measures for different aspects of liver function and are also indices of liver cell damage.

Biochemical Parameters Serum Enzymes Test

Alkaline phosphatase: Increased concentration of enzyme with higher doses of additive may be retaliatory action of the liver due to toxic action of the additive resulting in overproduction of alkaline phosphatase.

SGOT and SGPT: These two enzymes form a link between carbohydrate and protein metabolism. Liver has the largest concentration of both enzymes. The damage to the tissue may release these enzymes into the blood stream.

Protein: Decrease in the liver and serum content could be due decrease utilization of amino acids into protein and severe necrosis and degeneration of hepatic parenchyma cell.

Glycogen: Glycogen depletion reflects the lost capacity of the hepatocytes to metabolize glycogen normally because of the increased energy demand. As a result, cells rapidly loses glycogen causing a diminished glucogenesis from proteins in the liver.

Bilirubin: It is the major bile pigment and is derived from the metabolism of heamoglobin and other porphyrin compounds. An increase in serum bilirubin concentration is a sensitive indicator of liver disease i.e. hepatocellular dysfunction. Rise in bilirubin could be due to retention in the circulation of bilirubin.

Conclusions

In conclusion, long time intake of Aspartame causes functional, anatomical and physiological impairments. The damages, thus, caused are almost irreversible impairment to the homeostasis of the animal. These results suggest that community should minimize the use of low calorie sweetener i.e. Aspartame, because it’s intake is harmful. The effect of daily intake may not express in one or two years, but it may take 5, 10 or 15 years. Then it may become too late.
References