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Renal Histological Effects of Artificial Sweeteners in Albino Rats

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Abstract. The study was conducted to evaluate the effect of different doses of artificial sweeteners on the kidneys of male and female rats, and to identify the potential renal tissue damage effects. The study included (15) male and female rats that were subjected to the necessary laboratory conditions for 30 days. They were divided as follows: a control group; a group that was given one sweetener tablet dissolved in 2 cc of water at a rate of two doses of 1 cc for a month; and a group that was given two sweetener tablets dissolved in 4 cc of water at a rate of four doses of 1 cc for a month. Histological examination of the kidneys of rats treated with one and two sweeteners revealed tissue lesions in the cortex, fragmentation and atrophy of the glomerulus, expansion of the capsular or urinary space, desquamation of the epithelium lining the parietal layer of Bowman's capsule, and desquamation of the epithelial cells lining several urinary tubules. Hematomas were also present in some sections. The medulla also showed extensive hemorrhage around the urinary tubules and partial desquamation of the epithelium lining several urinary tubules. Our study concluded that the use of sweeteners containing sodium cyclamate and sodium saccharin is unsafe for the kidney and may cause renal tissue lesions over the long term.

Keywords: kidney, artificial sweeteners, sodium cyclamate, sodium saccharin

1. INTRODUCTION

Artificial sweeteners are very popular these days due to their low calorie content. Therefore, the food industry uses various types of low-calorie artificial sweeteners instead of high-calorie sugar [1]. The US Food and Drug Administration has approved the use of many sweeteners according to the acceptable daily value (ADI) [2]. However, the breakdown products of these sweeteners still cause health effects on the body's organs, especially the kidneys, and these effects are interesting. On the other hand, rare sugars are monosaccharides and have no known health effects because they are not metabolized in our bodies, but they provide the same sweet taste and texture as sugar. Rare sugars do not have this acceptable daily value and are mainly produced using bioreactors. Therefore, despite their high demand, their effects need to be more widely known [3,4]. Saccharin is the oldest non-nutritive artificial sweetener, with a concentration ranging from 300 to 500 mg. It is a highly stable compound with increasing heat and time, making it suitable for use in warm beverages and in food processing plants that require high temperatures for preparation, such as preserved vegetables, thickened jams, and bakery products [5]. There are a variety of saccharins, such as sodium saccharin, potassium saccharin, calcium saccharin, and acid saccharin. The most commonly used saccharin is sodium saccharin because it is so tasty [6]. The standard daily intake of saccharin is 2.5 mg/kg of body weight [7]. When ingested, saccharin passes through the digestive tract undigested, as studies have shown that saccharin is neither absorbed nor metabolized through the intestine [8-9]. Saccharin absorption occurs rapidly and is dependent on food intake. Once removed from food, it takes three days for it to be completely eliminated from tissues [10]. Continued consumption of saccharin

increases the risk of obesity and diabetes, as well as impaired liver and kidney function, and increases the risk of brain cancer[11] .

2. MATERIALS AND METHODS

2.1. Materials used in the experiment

A commercial sweetener called Merasweet was used. Each tablet contains 40 mg of sodium cyclamate, 4 mg of sodium saccharin, and 4.4 g of sugar, according to the label.

2.2. Experimental Design

Fifteen rats, aged 12 to 15 weeks and weighing between 300 and 400 g, were divided into four groups, with five animals per group, as shown below.

- The control group was given drinking water and food ad libitum for 30 days. The diet consisted of (20% yellow corn, 20% soybean meal, 30% corn gluten, 10% barley, 1% vitamin and mineral mixture, 1% limestone, 4% dicalcium phosphate, 5% table salt, 10% L-lysine monohydrochloride (10%), and methionine).
- The second group was given one tablet of the sweetener dissolved in 2 cc of water, at a rate of two doses of 1 cc each, for one month.
- The third group was given two tablets of the sweetener dissolved in 4 cc of water, at a rate of four doses of 1 cc each, for one month.

2.3. Tissue Section Preparation

Tissue sections were prepared using the Luna method [12] according to the following steps: (Fixation, Washing, Dehydration, Clearing, Infiltration, Embedding, Sectioning and Trimming, Staining, Mounting).

3. RESULTS

3.1. Control group

The kidney tissue of the control group was normal, containing normal-looking glomerulus and renal tubules, as shown in Figure (1, 2).

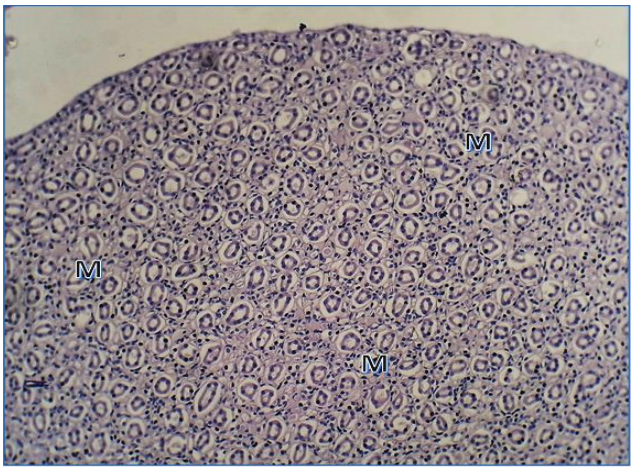

Figure (2): A microscopic image of a rat kidney from the control group, showing the medulla area and the normal appearance of the urinary tubules

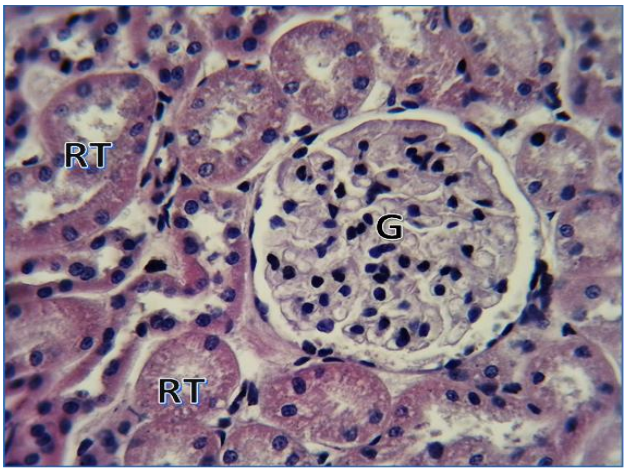

Figure (1): A microscopic image of a rat kidney from the control group, showing the normal appearance of the glomerulus (A) and renal tubules

throughout the tissue section. (H&E, X100).

(RT). (H&E, X400).

3.2. The group treated with a single sweetener

The results showed that the cortex contained a lobulated or fragmented glomerulus, with dilatation of the capsular or urinary space, desquamation of the epithelium lining the parietal layer of Bowman's capsule, and desquamation of the epithelial cells lining several urinary tubules. Hemorrhages were also present in some sections. The medulla contained extensive hemorrhage around the urinary tubules and partial desquamation of the epithelium lining several urinary tubules (Figures 3 and 4).

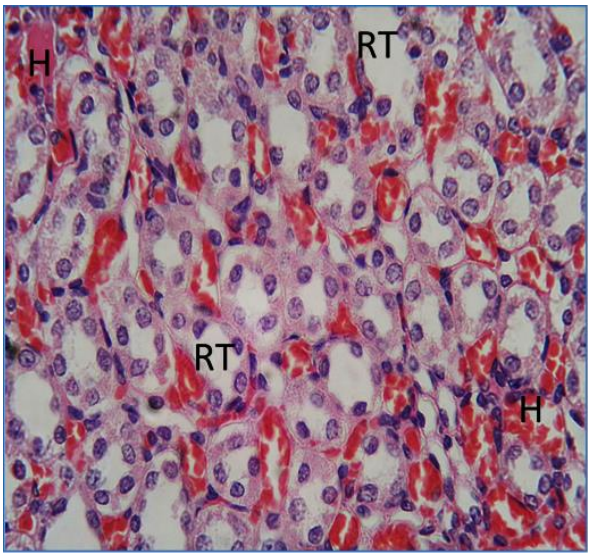

Figure (4): A microscopic image of a rat kidney from the group treated with a single grain of the sweetener, in which the medullary area is observed to contain extensive hemorrhage around the urinary tubules (H), partial desquamation of the epithelium lining a number of urinary tubules (RT), (H&E, X400).

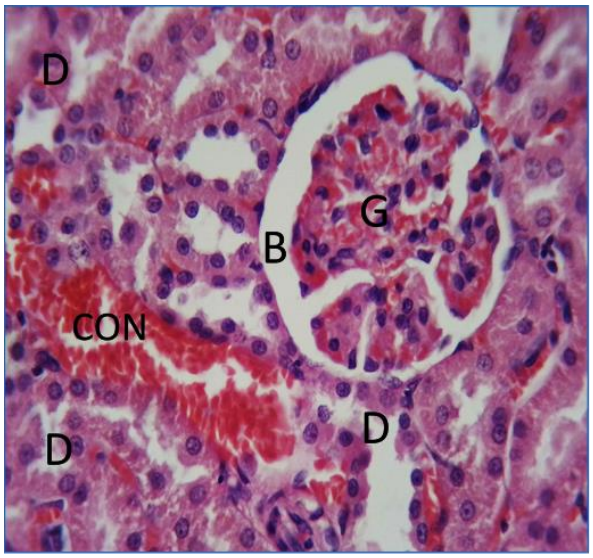

Figure (3): A microscopic image of a rat kidney from the group treated with a single grain of the sweetener, showing the cortex area containing a segmented glomerulus (G), expansion of the capsular or urinary space (B), desquamation of the epithelial cells lining a number of urinary tubules (D), with blood congestion (CON). (H&E, X400).

3.3. *The group treated with two sweeteners*

The results shown in Figures 5 and 6 showed that the cortex contained an atrophic glomerulus with dilated capsular space, desquamation of the epithelium lining the parietal layer of Bowman's capsule, and desquamation of the epithelial cells lining several urinary tubules. There was also blood congestion in some sections. The medulla contained extensive hemorrhage around the urinary tubules and partial desquamation of the epithelium lining several urinary tubules.

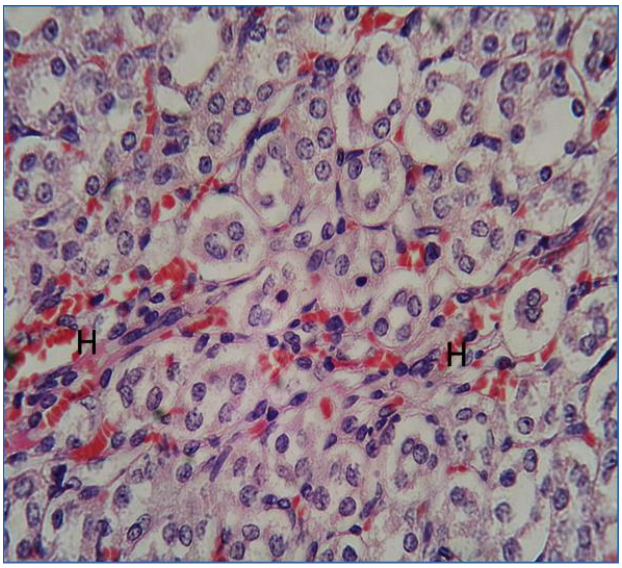

Figure (6): A microscopic image of a rat kidney from the group treated with two granules of the sweetener, in which bleeding (H) is observed in the pulp area throughout the tissue section. (H&E, X400).

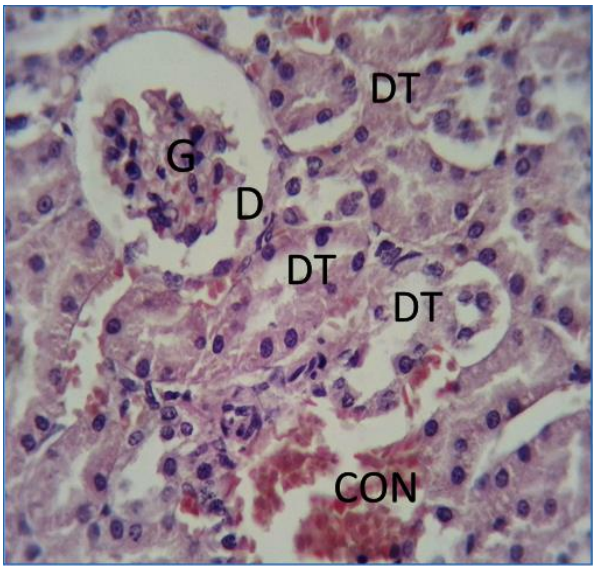

Figure (5): A microscopic image of a rat kidney from the group treated with two granules of sweetener, showing atrophied glomerulus (G), expansion of the capsular space, desquamation of the epithelium lining the parietal layer of Bowman's capsule (D), partial desquamation of the epithelium lining a number of urinary tubules (DT), and blood congestion (CON) (H&E, X400).

4. DISCUSSION

Histological examination of the kidneys of rats treated with one and two sweeteners revealed histological lesions in the cortex, fragmentation and atrophy of the glomerulus, dilatation of the capsular or urinary space, desquamation of the epithelium lining the parietal layer of Bowman's capsule, and desquamation of the epithelial cells lining several urinary tubules. Hematomas were also present in some sections. The medulla showed extensive peritubular hemorrhage and partial desquamation of the epithelium lining several urinary tubules. These lesions may be due to the presence of sodium saccharin, although several artificial sweeteners are approved by the FDA, including saccharin, acesulfame, aspartame, neotame, and sucralose. Although the most common sweetener is sodium saccharin, due to its pleasant taste [13], due to its pleasant taste, large quantities of it are consumed in sweet foods and beverages, which were used in our current experiment. Other studies, consistent with our study [14], have shown that sodium saccharin causes damage to cell membranes through peroxidation, ultimately leading to tissue necrosis and cell death. In order to learn more about the toxic effects of artificial sweeteners, the aim of the current work was to provide improved information regarding the toxic potency of saccharin, particularly the mechanisms leading to kidney toxicity and kidney dysfunction. The histopathological effects of saccharin on the kidneys of laboratory animals treated with different amounts of sodium saccharin were evaluated after 30 days. In this study, treated rats showed significant cellular damage in the liver and kidneys according to the dose. Furthermore, saccharin is not absorbed or metabolized throughout the human and animal gastrointestinal tract, so it is excreted by the kidneys unchanged. Based on this reason, the US Food and Drug Administration (FDA) has ruled that saccharin is not hazardous [15, 16]. These findings differ from our findings, as studies have shown that sodium saccharin may cause oxidative stress on hepatocytes by reducing catalase activity and decreasing total plasma antioxidant concentrations [17, 18]. Saccharin has been shown to have a destructive effect on both the cortex and medulla of the kidney [19]. Our findings are consistent

with those of Usman [20], who reported that sodium cyclamate ingestion may cause histological lesions and inflammation in the kidney.

5. Conclusions

The use of sweeteners containing sodium cyclamate and sodium saccharin is not safe for the kidney and may cause tissue lesions in the long term.

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