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Research Article

Non-Nutritive Sweeteners Modulated Creatinine and Urea Levels in White Albino Rats

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ABSTRACT

Artificial sweeteners, also known as nonnutritive sweeteners have many benefits like low calories count. It is frequently used for reducing weight, controlling blood sugar levels and decreasing the chances of dental decay. This study evaluated the effects of NNS in the kidney function. Using the blood sample of the albino rats, the level of creatinine and urea was calculated after the use of NNS for 3 weeks. 70 rats were equally divided into 7 groups. The groups were given Stevia 200mg/kg/day, 10% solution of sucrose, Sucralose 3g/kg/day, Saccharine, Aspartame 250mg/kg/day and Acesulfame-k 250mg/kg/day respectively. In the controlled group, distilled water was used as a placebo. The results indicated that saccharin and aspartame both caused the urea to increase to 37±0.5 mg/dl from initial 30±1.5mg/dl and acesulfame-k represented the most increase in the urea, which elevated the levels from 30 mg/dl to 38±1.5 mg/dl. Additionally, saccharine and aspartame increased the creatinine levels from from 0.1 to 0.85±0.05 mg/dl and sucralose elevated the level of creatinine from 0.1 mg/dl to 1.3±0.2 mg/dl. In the stevia group, the results remained the same as in the controlled group. This indicates the nephrotoxic effects of NNS and proves Stevia safe for the daily use as an alternative.

Key words: Artificial sweeteners, Non-nutritive sweeteners, Acesulfame-K, Aspartame, Saccharine, Sucralose.

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INTRODUCTION

Currently it has been observed that many synthetic products which are labeled as low caloric or low fat products are in high demand of public use. One of the most leading products of this category are the sugar free products.[1] Multiple edibles like jams, ice-creams, jellies, candies, biscuits, dairy products etc. are available under this label. All these products use artificial sweeteners as the replacement to high caloric sugar in the form of sucrose or glucose.[2,3] this use of alternative sweeteners have enabled the sweet products to be low fat and sugar free.

Artificial sweeteners, also known as nonnutritive sweeteners have many benefits which includes, the low or zero calories count.[4] This helps the people to control the increase in weight and also reduce the body weight. With the increase in the prevalence of obesity it has gained high popularity in the recent times. Secondly, these alternatives to sugar helps in controlling the hyperglycemia and reduces the blood sugar levels.[5,6] Therefore, it is consumed by many diabetic patients and they have observed promising results in diabetes control, when patients intake these sweeteners instead of the conventional sugar. Commonly sold non-nutritive sweeteners are, stevia, sucralose, saccharine, aspartame, and acesulfame-k. It has been indicated that these sweeteners are safe for the daily use which permits its' use in everyday as an alternate to the sugar.[7,8]

However, the increase use of these sweeteners are under high interest of studies as the use is growing day by day. Some of the reported adverse effects associated with the nonnutritive sweeteners are, negative metabolic effects, hepatotoxicity, oxidative stress on the liver, increase in body weight, increase risk of diabetes mellitus, inflammation, disturbance in insulin homeostasis, etc.[9,10]

The potential relationship between the sweeteners and sugar with the injury to kidney could be linked with many risk factors like gout, diabetes, and acute kidney injury.[11,12] The possible pathway can be excretion of these molecules through kidney eventually damages the renal function, which in many ways increases the chances of chronic kidney disease[13]. We aimed to evaluate the effect of non-nutritive sweeteners including stevia, sucralose, saccharine, aspartame, and acesulfame-k on the kidney function test and to compare the effects of non-nutritive sweeteners with the effects of sucrose in kidney function test.

MATERIALS AND METHODS

Animals: This study has used the Albino rats who weighted between 250g to 300g and aged between 3 to 4 weeks old. These rats were kept under the controlled environment at the set temperature of 20 to 24 ◦C with humidity (65%) and 12 hours light and 12 hours dark cycle. Food and filtered water was supplied to the rats as per need. All animals were kept under the protocols of animal's ethics committee.[14,15]

Experimental groups: The randomized controlled trial was held for the period of 90 days. 70 rats were divided equally into seven groups. Rats of each group were given the respective drug or the placebo. Timely analysis of each rat was done and recorded.

Chemicals: Tested group given, Stevia 200mg/kg/day, 10% solution of sucrose, Sucralose 3g/kg/day, Saccharine, Aspartame 250mg/kg/day and Acesulfame-k 250mg/kg/day. Distilled water has been used as the placebo in the control group.

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Sample collection: To evaluate the renal function of the rats the blood sample was collected and the levels of serum urea and creatinine were recorded for each group separately.[16,17]

Statistical analysis: All the result were presented in bar graphs with respect to each group individually. The differences were studied using one-way analysis of variance (ANOVA) and Fisher test (Stat View). All the values were statistically significant with $p \leq 0.05$.

RESULTS

After twelve weeks of the administration of the respective agents in the rats, the urea analysis have shown the following results. The control group which was given the distilled water remained constant before (32±2) and after (33±2.5) the experiment. In sucrose group, the results remained almost the same too. This represents that both that placebo and sucrose did not influence the renal function at all. In stevia group the results were nearly similar to the results of sucrose group. Sucralose increased the urea level from 31±2 mg/dl to 36±1 mg/dl. Saccharin and aspartame both caused the urea to increase to 37±0.5 mg/dl from initial 30±1.5mg/dl. Lastly, acesulfame-k represented the most increase in the urea, which elevated the levels from 30 mg/dl to 38±1.5 mg/dl.

Through the renal function test, on the analysis of the creatinine after the administration of the treatment agent the following results have been found. In the control group, sucrose group, and stevia groups; the results of before and after remained the same; close to 0.1mg/dl. This states that similar to the distilled water, sucrose and stevia did not have any negative impact of the kidney and it did not affect the level of creatinine entirely. In case of sucralose, the level of creatinine markedly increased from 0.1 mg/dl to 1.3±0.2 mg/dl. Saccharine also increased the levels from 0.1 to 0.85±0.05 mg/dl. Aspartame have shown the similar results too; the creatinine level increased from 0.1mg/dl to 0.89±0.05 mg/dl. There was a slight increase in the acesulfame-k group which was from 0.1 mg/dl to 0.390.85±0.05 0.04 mg/dl (figure 1).

DISCUSSION

One of the most important and prominent function of kidney includes the removal of waste products from the body. Excretion of toxic substances from the body in form of urine is the major role of kidney. This leads to the understanding of the nephrotoxic effects of the artificial sweeteners.[18] As the acidified molecules is in taken by the body, it tends to add stress on the kidneys which eventually leads to acute kidney injury and chronic kidney diseases.[19]

The results of this study demonstrates that stevia, an artificial sweetener is safe and secure for the use in diet with respect to its impact on the functions of kidney. It was found that it did not contribute to the increase in creatinine and urea. A similar study has been conducted to evaluate the impact of the stevia sweetener on the mice with chronic kidney disease. 50 mice were divided into five groups, 10 mice in each. The groups were as follows, Normal controlled group, Model controlled group, Positive control group, Stevia residue extracts 200 mg/kg group and Stevia residue extracts 400 mg/kg group. The urine sample and blood sample of the mice were collected and evaluated. The final results represented that the stevia residue extracts had the potential to reduce the kidney injury which was resulted due to adenine. The following study clearly showed the renoprotective impact of the stevia.[20] Several other studies have seconded these results and declared stevia as a safe product.

In case of saccharine, the results have shown marked increase in both the urea and creatinine. Another study which evaluated the results of saccharine use as a sweetener and food flavor on the albino rats examined the effects on the total cholesterol, glucose level, triglycerides and weight gain, renal function and hepatic function. The results of this study stated that, saccharine at both the high and the low doses resulted into increased level of liver enzymes and destructively altered the biochemical markers in kidney. However, in another study it has been stated that saccharine is absorbed in the gut at a slower rats and it actively and easily passes out of the body through urine. Although the saturation in the renal tubules was found in rats but it was not fund in humans in case when the volunteers were given 2g of saccharine orally. Similarly, another study on the albino rats also evaluated the effects of saccharine and sucralose in the physiological parameter, it too ideated that the use of saccharine for a longer duration results into adverse effects on the kidney and liver function.[21]

Aspartam has shown representedly a remarkable drawback on kidney function and this findings further supported by alternative studies who have reported a dedicated effects on this sweetener on kidney dysfunction.[22-26] Close likely is acesulfame-K studies which have indicated that kidney injury is possible plausible result from chronic intake of acesulfame-K containing products.[26,27]

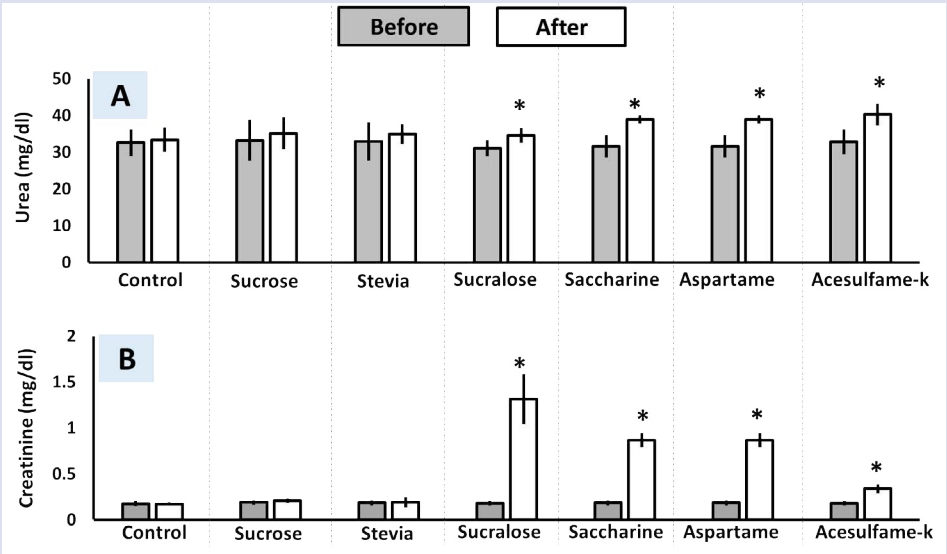

Figure 1: Artificial sweeteners (AS) modulated renal function tests in experimental rats in AS-exposed group as compared to negative and positive. The data expressed as mean±SD, *p<0.05 significant compared to after exposure.

It has been stated the use of sucralose as a sweetener and an alternate to the sucrose has resulted into multiple side effects.[28] The histopathological images of liver and kidney tissues represented the severe damage to the cell morphology. Furthermore, the elevation in the levels of immunoglobulin and pro-inflammatory cytokines were also reported. This study also represents the similar results and highlights the marked increase in the urea and creatinine levels.[29]

CONCLUSION

The use of artificial sweeteners has markedly increased in the recent times. It provides the taste similar to that of the sugar but it has low or no calories which help in reducing the weight, controlling blood sugar level, decreasing the chances of dental problems, and improving the quality of life and reducing the impact on chronic diseases. However, there are many side effects associated with the use of non-nutritive sweeteners. Through these results it has been found that the use of NNS causes the increase in urea and creatinine which eventually leads to kidney damage. However, stevia has been proven to be safe which presented the levels same as the controlled group.

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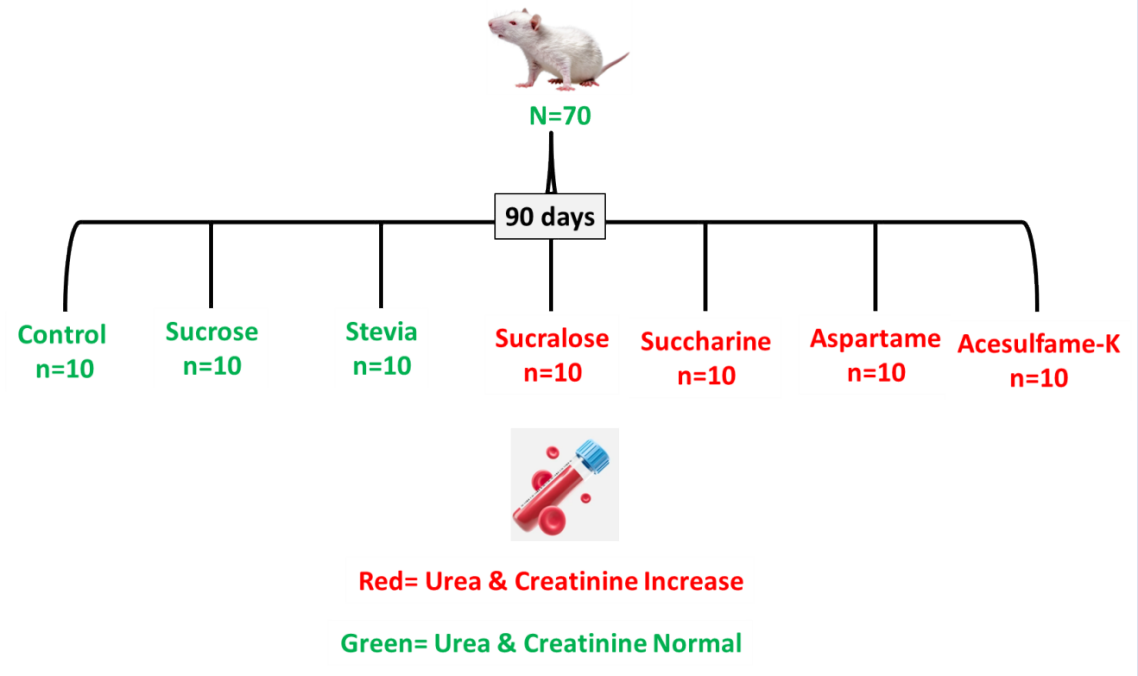
GRAPHICAL ABSTRACT



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