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CHARACTERIZATION OF FRUCTOSE DIET INDUCED DIABETES MELLITUS IN SWISS ALBINO MICE

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ABSTRACT: Diabetes mellitus is an endocrine disorder, in which a person has high blood sugar, and the body does not produce sufficient insulin, or cells do not act in response to the insulin that is produced. Diabetes mellitus is a complicated metabolic disease that has gravely affected the human health and quality of life. As increase in carbohydrate intake, especially of fructose and high rich diet are both factors that contribute to the development of diabetes mellitus. In the present study, the characterization of fructose diet induced diabetes mellitus in Swiss albino mice was studied. Animals were divided into two groups, group A (Control) and group B (Fed with fructose diet). Oral administration of 10% fructose solution to Swiss albino mice for 10 weeks resulted in diabetes mellitus. For the duration of the experiment bodyweight, fasting blood glucose level and biochemical parameters (total cholesterol, total serum protein, serum creatinine and blood urea) were measured. The study revealed that fructose diet resulted in significant increase in bodyweight, fasting blood glucose level, total cholesterol, creatinine and blood urea. However, total serum protein in fructose fed mice group decreased significantly as compared to control. It is concluded from the experimental study that fructose diet increase glucose level, biochemical parameters and cause diabetic in Swiss albino mice.

INTRODUCTION: Diabetes mellitus is chronic metabolic disorders that have an effect on human body in stipulations of psychological, physical and social health. Diabetes mellitus, often simply referred as diabetes. Diabetes is becoming the third 'killer' of the welfare of mankind along with cardiovascular, cerebrovascular and cancer diseases because of its high prevalence, mortality and morbidity[1]. Diabetes mellitus is a chronic disorder of carbohydrate; lipid and protein metabolism characterized by increased fasting and post prandial blood sugar level [2]. It is a universal endocrine disease in which there occur increased foods and water intake [3].

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Diabetes mellitus (DM) is a group of metabolic disorder characterized by chronic hyperglycemic condition resulting from defects in insulin action, insulin secretion or both [4]. Diabetes is definitely one of the challenging health problems in 21st century. Diabetes in all its form imposes unsuitably high human, social and economic costs on countries at all income levels.

According to the sixth edition of the world Diabetes Atlas released by the International Diabetes Federation (IDF), the majority of the 382 million live with diabetes, which is set to increase to 592 million people causes diabetes by 2035. However, with 175 million of cases presently undiagnosed, an enormous amount of people with diabetes are moving ahead towards complication unaware. Furthermore, with 80% of entirety affected livelihood in middle and revenue countries, all types of diabetes are on the increase, type 2 diabetes especially and the number of people

with diabetes will enhance by 55% by 2035. There is one person in the world dying of diabetes every six seconds by the worst affected are people in the age group of 40 to 59 years [5]. A person with diabetes does not absorb glucose properly, and glucose remains circulating in the blood (a condition known as hyperglycaemia) damaging body tissues over time. This damage can lead to disabling and life- intimidating health complications [5].

The diabetes are referred as type 1 (insulin dependent) and type 2 (non-insulin dependent) [6]. Type1 diabetes is caused by autoimmune response, where the body's protection system attacks the insulin-produces beta cell in the pancreas and as a result, the body can no longer generate the insulin it desires. The syndrome can have an effect on people of whichever age, other than generally occurs in young adults or children [5]. Type 2 diabetes is most common type of diabetes. It is generally occurs in adults, but is ever more seen in children and early existence. In diabetes mellitus, the body is up to produce insulin but either this is not enough or the body is not capable to respond to its effects (also known as insulin resistance), leading to a buildup of glucose in the blood.

Many people with diabetes mellitus stay behind unaware of their disease for a long time as symptoms may take years to emerge or be recognized, for the duration of which time the body is being damaged by excess blood glucose [5]. Type 2 diabetes is nearing epidemic proportions as a result of increased number of elderly people and a greater frequency of sedentary lifestyle and obesity. The cause of diabetes is a mystery, although both environmental and genetic factors such as obesity, unsatisfactory diet and lack of exercise to play a role [1].

Non-genetic environmental factor counting food and diet constituents are able to preclude or induce numerous diseases [7, 8]. The incidence of metabolic syndrome has spectacularly augmented worldwide due to a modern life style [9] and enhances of consumption of high sugar diets in particular fructose [10]. As a result, elevating of effectual dietary compounds is necessary.

Fructose is a usual sugar and is commonly used as a sweetener [11]. Fructose is readily engrossed and rapidly metabolized by human liver. Fructose feeding has been shown to wield harmful effects and promote oxidative damage by reducing antioxidant defenses, and escalating generation of free radicals [12]. Fructose is an imperative dietary source of carbohydrates. Fructose is an isomer of glucose with a hydroxyl group on carbon- 4 reversed in positions [13]. Fructose is a universal monosaccharide that is found naturally in its gratis form in fruits, honey, and other plants and in a combined form as half of the disaccharide sucrose.

Fructose is used widely in carbonated beverages, canned fruits, jams, dairy products and baked goods [14]. It is known that, extreme fructose utilization perhaps responsible in part for the rising incidence of diabetes mellitus, non-alcoholic fatty liver disease, obesity and cardiovascular diseases [15]. Earlier studies reports are accessible on the effect of fructose in rats and other rodents. However, no data about the effect of fructose diet in mice. The aim of the present study was designed characterization of fructose diet induced diabetes mellitus in Swiss albino mice.

MATERIAL AND METHODS:

Chemicals: Fructose and all the chemicals used in the experiments were of analytical grade and purchased from Himedia Laboratories Private Limited. (Mumbai, India).

Animals: Swiss albino mice (6-7 week old weighing approximately 25-30 gm) were housed in polypropylene cages (3 animals per cage). The animals were kept during the experiment for full acclimatization in an air-conditioned animal room (25± 2ºC) under a 12 h light/dark cycle. The animals had free access to standard pellet diet and water.

All experimental procedures were performed in accordance with the recommendations found in the Guide for the Care and Use of Laboratory Animals [16] and approved by the institutional Animal House and Use Committee of the Jayoti Vidyapeeth Women's University of Jaipur. Institutional ethical guidelines were also followed in all Experiments.

Induction of diabetes mellitus in mice:
Diabetes were induced in Swiss albino mice by feeding 10% fructose solution in water for 10 week that was prepared every day.

Experimental design: The mice were divided into two groups comprising of 3 animals in each group as follow:-

Group I: - Control normal mice, received water and fed with standard pellet diet.

Group II: - Fructose fed mice, fed with 10% fructose solution for 10 week.

Experimental procedure:
Blood glucose Estimation:
Blood was drawn from the tail vein of mice with the help of sharp needle and blood glucose level was measured every other week by using glucometer (One ultra touch, Johnson and Johnson).

Bodyweight Estimation:
All animals were weighed every two weeks until the end of the experimental protocol.

Biochemical Estimation: The experiments were carried out for 10 weeks. During the experiment blood sample were obtained after the overnight from the tail vein of all the animals. Blood was left to clot and was centrifuged at 3000 rpm for 15 min. at 4°C for separating the serum which was frozen and stored at -20°C until biochemical analysis serum cholesterol (Zak's method), total serum protein (Lowry method); serum creatinine (Jaffe method) and blood urea level (DAM-TSC method) were performed.

Statistical analysis:
All result are presented as mean±SEM. To determine the significant differences between the two groups were calculated using student t- test. *P* values of less than 0.05 were considered to be significant. All analyses were performed using IBM SPSS Statistics 20.

RESULTS:
The effect of fructose on body weight of mice group during the experimental period are represented in **Figure 1; Table 1**. During the 10 week of experiment, the weight of fructose fed mice group (27.12±0.12) slightly significantly increased from the first week until the end of the experiment when compared with control group (34.78 ± 0.66) ($p<0.05$).

Table 2 shows the effect of fructose on fasting blood glucose level of mice. Blood glucose in fructose fed mice group (92 ± 2.08) increased significantly with respect to the control group (167±1.63) ($P<0.05$); **Figure 2**.

TABLE 1: THE EFFECT OF FRUCTOSE ON BODY WEIGHT IN CONTROL AND EXPERIMENTAL GROUP

Weeks	Control	Diabetic Mice
0 day	26.2±0.41	26.16 ± 0.34
week 2	26.17±0.31	27.28 ± 0.42
week 4	27.2± 1.14	29.34 ±0.84
week 6	26.64±0.41	31.05 ± 0.61
week 8	28.47±0.44	32.85 ± 0.63
week 10	27.12±0.12	34.78 ± 0.66*

Values are shown as the mean±SEM. Values are statistically significant at * $p<0.05$ when compared to normal/control group.

TABLE 2: THE EFFECT OF FRUCTOSE ON FASTING BLOOD GLUCOSE LEVEL IN CONTROL AND EXPERIMENTAL ANIMAL

Weeks	Control	Diabetic Mice
0 day	89.66±1.45	94.33± 2.72
week 2	94.33±3.17	115.66±4.05
week 4	93±4.04	128±1
week 6	87.66±5.6	142.33±2.02
week 8	95.66±2.02	155.66±1.63*
week 10	92±2.08	167±1.73*

Values are shown as the mean±SEM. Values are statistically significant at * $p<0.05$ when compared to normal/control group.

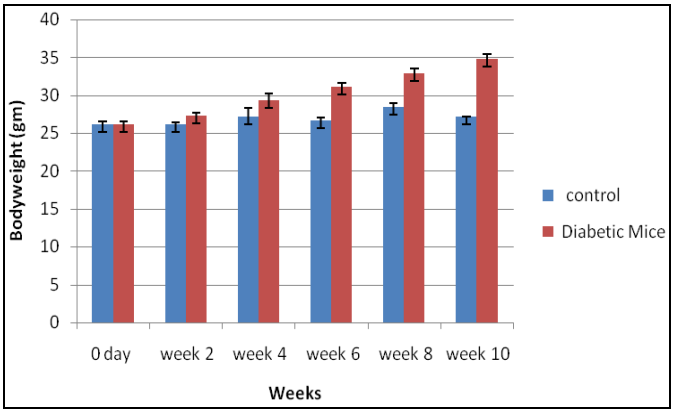

FIG 1: SHOWING THE EFFECT ON BODYWEIGHT OF CONTROL AND FRUCTOSE TREATED MICE

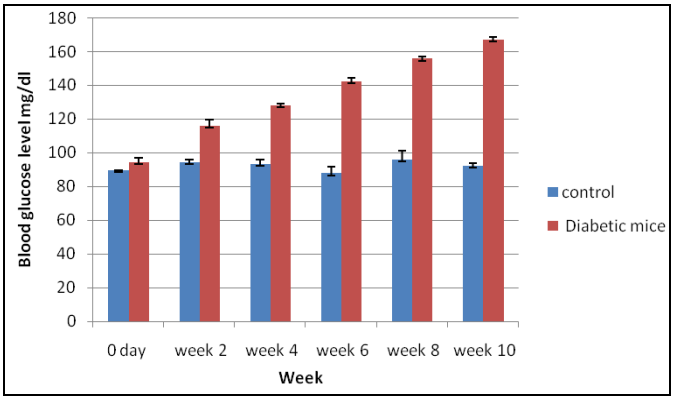

FIGURE 2: SHOWING THE EFFECT ON FASTING BLOOD GLUCOSE LEVEL OF CONTROL AND FRUCTOSE TREATED MICE

The mice fed fructose showed a significant increase of cholesterol (89.22± 1.17; 143.07± 1.93) with ($p<0.05$), serum creatinine (0.60± 0.04; 5.62± 0.11) with ($p<0.05$) and showed a significantly decrease of total protein (5.63± 0.10; 3.08± 0.05) with ($p<0.05$) as compared to the control group.

Fructose induced mice were found to have significantly elevated blood urea level (56.74± 1.87) with the respect to the control group (26.9± 1.47) ($p<0.05$) **Table 3**.

TABLE 3: THE EFFECT OF FRUCTOSE ON FASTING TOTAL CHOLESTEROL, SERUM PROTEIN, SERUM CREATININE, BLOOD UREA IN CONTROL AND EXPERIMENTAL ANIMAL

Groups	Total Cholesterol mg/dl	Serum Protein g/dl	Serum Creatinine mg/dl	Blood Urea mg/dL
Control	89.22± 1.17	5.63± 0.10	0.60± 0.04	26.9± 1.47
Diabetic Mice	143.07± 1.93*	3.08± 0.05*	5.62± 0.11*	56.74± 1.87*

Data are shown as the mean±SEM. Values are statistically significant at * $p<0.05$ as compared to normal/control group.

DISCUSSION:

Diabetes mellitus, a pervasive and multifactorial metabolic disorder, is characterized by imperfection in insulin receptor or post receptor and insulin secretion events with derangement in protein, carbohydrate and lipid metabolism [17]. Patient with diabetes are at augmented risk of atherosclerosis and its clinical squeals: coronary, renal, peripheral vascular and cerebrovascular diseases. At the same time as, the most common cause of death in person with diabetes is myocardial infarction.

The pathogenesis, progression and epidemiology of atherosclerotic disease are distinct in patients with diabetes [18]. Diabetes mellitus patients in India are raising day by day most likely as a result of change in way of life modify in food pattern that is from traditional sugary fast food diet to fiber rich diet and also as of genetic basis [19]. Fructose is potent reducing sugars that promote the formation of toxic advanced glycation ending products, which become visible to be part of the cause in the aging process; in the pathogenesis of the renal, ocular and vascular complications of diabetes [20].

In addition, excessive fructose consumptions may be responsible in part for the escalating incidence of obesity, non-alcoholic fatty liver disorder and diabetes mellitus characterized by an impaired glucose tolerance test. With a few exceptions, the quite small amounts of fructose those happen naturally in vegetables and fruit are unlikely to have harmful effects [21]. In this study, the characterization of fructose diet induced diabetes mellitus in Swiss albino mice on some biochemical parameters of the blood glucose level, bodyweight, serum cholesterol, serum total protein, serum creatinine and blood urea level were investigated.

There was no death recorded during the course of the experiment in group. In the current study the induction of type 2 diabetes following 10 weeks treatment with fructose. The result of the present study showed that the mice fed with 10% fructose solution for a period of 10 weeks which induces diabetes mellitus. As indicated in previous studies on rats and other rodents [22].

In another report, a 10% fructose for 21 days induced glucose intolerance in rats [23]. It has been reported that metabolic syndrome was induced in Wister rats by feeding 10% fructose solution for 8 week [24]. On the other hand, it has been showed that 10% fructose to Wister rats for 30 days resulted in hyperglycemia and hyperlipedemia [25]. This in agreement with the finding of who reported that fed fructose for 10 days resulted insulin resistance in rats [26]. In a more recent study, a 10% fructose solution for 8 weeks has been shown to induce

diabetes mellitus type 2 in Sprague- Dawley rats [27]. To our knowledge, this is the first report showing that 10% fructose solution fed in Swiss albino mice and found the changes in lipid profile. Profound changes in protein metabolism occur in Diabetes mellitus. Enhanced catabolism of muscle proteins in diabetes elevates the serum creatinine level [28].

In our study fructose diabetic mice showed a significant increase in serum creatinine, blood urea level and decrease serum protein level as compared to control group. Previous studies showed that significantly increase in plasma total protein level, urea and creatinine level in diabetic albino rats [29]. Although there are a few studies exploratory the effects of fructose consumption on bodyweight, these reports are first and foremost descriptive and results are at variance. In the present study fructose fed mice showed significant and consistent increase in fasting blood glucose level and it significantly increase the bodyweight at different intervals through the period of experiment as compared to control group.

In context other workers have been reported in rats that the significant increase in fasting blood glucose level and bodyweight [24, 25, 27]. In the present investigation fructose induced diabetic mice found to produce increase in total serum cholesterol and other lipid profile while correlates with earlier finding that there is an increase in lipid level total cholesterol is observed in diabetic Sprague-Dawley rats [27].

CONCLUSION: The study proved that 10% fructose fed Swiss albino mice successfully induced type2 diabetes. It is simple to expand, economical and can be used by researcher worldwide in particularly in developing countries, where resources and financial support are limited. As neither special formulation of diet nor sophisticated instruments are required, this model can be developed in animal laboratories with minimum facilities.

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