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# EFFECT OF SOME DIETARY NUTRITIVE SWEETENERS ON HEALTHY AND DIABETIC RATS

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## SUMMARY

The present work was performed to study the effect of feeding three different sweeteners on healthy and alloxan-diabetic rats. Thirty six female albino rats (mean weight was 147.9 ± 16.83 g) were divided into six homogenous groups of which three control groups and three alloxan diabetic groups. All the groups were fed on basal diet in combinations with 10 % either surcose, fructose or sucrol. Food and tap water were provided ad libitum for 28 days. The results revealed that, the lowest value of serum glucose was noticed in alloxan-diabetic group that received 10 % fructose than did the corresponding alloxan-diabetic groups. While the highest value of serum glucose was observed in 10 % sucrose alloxan-diabetic diet. Using 10 % fructose alloxan-diabetic diet, there were significant increase in ALT, total cholesterol, triacylglycerols, HDL-C and LDL-C ($P < 0.01$) as compared with healthy control basal diet. Also it is clear that, the rats consuming 10 % sucrol alloxan-diabetic diet exhibited non significant decrease in all biochemical analysis, except serum glucose and LDL-C as compared to either sucrose or fructose alloxan-diabetic diets. It was concluded that, sucrose, a high glycemic index should be avoided, in most non-insulin dependent diabetic patients. The availability of sucrol may enable patient to substationally liberalize the diabetic diet.

## INTRODUCTION

Nowadays, there is an increase in consumption of sucrose alternatives allover the world, where many people had realized the harmful effect associated with increased consumption of sucrose (Yoshihisa, 1989). Sugar alcohols (polyols), includeing sorbitol, xylitol, mannitol, mallitol, lactitol and hydrogenated glucose syrup (Salminen et

al., 1985), are considered nutritive sweeteners belonging to flavouring agents and the latter is subcidiary branch of food additives.

Sorbitol is one of the most widely found sugar alcohols in nature with relatively high concentrations occurring in apples, pears, plums, peaches and apricots (Wronstadt and Schellenberger, 1981). In comparison to sucrose, the relative sweetness of sorbitol is approximately 50 % (Sicard and Leroy, 1983). Whilst, Moore et al. (2001) observed that low dose of fructose improves the glycemic response to an oral glucose load in adults with type II diabetes and this effect is not a result of stimulation of insulin secretion. So, the main objective of this study was to investigate the effect of some nutritive sweeteners on performance of rats, relative organs weight and some clinical biochemical parameters in serum of healthy and diabetic rats.

## MATERIALS AND METHODS

### Materials :

The nutritive sweeteners used in the diets sucrose, fructose and sucrol (sorbitol and mannitol (1:1)] were purchased from supermarket.

### Experimental animals :

Six groups of female albino rats Sprague-Dawley strain of mean weight (147.9 ± 16.83) were used. They were obtained from Helwan breeding farm, Cairo, Egypt. The animals were divided into six groups and housed individually in stainless steel cages with wire mesh bottoms and maintained temperature and humidity controlled animals f cilities on a daily photo period of 12 h light a dark.

### Experimental diets :

The rats were fed on basal diet according to (All 1993) for four weeks, three groups were injecte intraperitoneally with alloxan (100 mg/kg boc weight) and classified as following :

Group 1 : the basic diet + 10 % sucrose.
Group 2 : the alloxan diabetic basic diet + 10 % sucrose.
Group 3 : the basic diet + 10 % fructose.
Group 4 : the alloxan diabetic basic diet + 10 % fructose.
Group 5 : the basic diet + 10 % sucrol.
Group 6 : the alloxan diabetic basic diet + 10 % sucrol.

Food and tap water were provided adlibitum Body weight gain and food consumption were recorded periodically.

### Samples :

**(1) Blood :**

At the end of the experiment, rats were sacrifie under ether anesthesia and blood samples wer obtained from hepatic portal veins. Serum wa separated and stored at – 20∞ till analysis.

**(2) Tissue :**

Liver, kidney, spleen and heart were removed and

ashed in saline solution, then dried on filter aper, weighed separately to calculate the abso- ute and relative organ weight.

**iochemical determinations :**

- Serum activities of aspartate aminotransferase (AST) and serum alanine aminotransferase (ALT) were estimated by colorimetric procedures kits developed by Diamond Diagnostics, Egypt according to Reitaman and Frankel (1957).

2 – Serum glucose concentration was determined by enzymatic colorimetric method kits developed by Randox Company, United Kingdom, according to Teuscher and Richterich (1971).

3 – Serum total lipid was determined using colorimetric method kits developed by Randox Company, United Kingdom, according to Schmit (1964).

4 – Serum triacylglycerols level was determined using enzymatic colorimetric method kits developed by Randox Company, United Kingdom, according to Trinder (1969).

5 – Serum total cholesterol was determined using enzymatic colorimetric method kits developed by Randox Company, United Kingdom, according to Trinder (1969).

6 – Serum HDL-cholesterol was determined using colorimetric method kits developed by Randox Company, United Kingdom, according to Arcol (1989).

7 – Serum VLDL-cholesterol and LDL-cholesterol were calculated according to Friedewald et al. (1972).

$$\text{VLDL-cholesterol (mg/dl)} = \frac{\text{Triacylglycerols (mg/dl)}}{5}$$

LDL-cholesterol (mg/dl) = total cholesterol – (VLDL-C + HDL-C)

**Statistical analysis :**

Statistical analysis was done by completely randomized design in factorial arrangement (ANOVA, F-test, L.S.D) showed evidence of over differences between diets according to Winer (1971).

## RESULTS AND DISCUSSION

The results tabulated in Table (1) showed the effect of feeding dietary different sweeteners on body weight gain, feed efficiency and relative weight of organs. From this table it is clear that, significant decrease was observed in body weight gain in alloxan-diabetic rats, which given 10 % sucrose ($P < 0.01$) as compared with its corresponding healthy control group that given the same 10 % sucrose. But in another way, alloxan-diabetic rats, which was fed on 10 % either fructose or sucrol had non significant increase in body weight gain than did the corresponding controls.

The reduction of weight in alloxan-diabetic group that received 10 % sucrose may be interpreted on the basis that, in diabetic with insulin deficiency, lipase activity increases, resulting in enhanced lipolysis (Harper's 1996). But the increase in body weight gain in diabetic groups that received either sucrol or fructose may be due to the increased utilization of fructose and sucrol than sucrose in diabetic rats, and sucrol and fructose are independent of insulin. The results also showed that, there were significant difference in the mean values of feed efficiency throughout all groups. The present results were found to be related with those reported by Ellwood et al. (1999) who studied the effect of dietary xylitol or sorbitol on rats and found that, the addition of sugar alcohols decreased food efficiency and total body weight gain regardless of the type fed.

**Table (1): Effect of dietary different sweeteners on body weight gain, feed efficiency and relative weight of organs.**

| Groups | Weight gain (g) | * Feed efficiency | Relative weight of organs (g %) | | | |
|---|---|---|---|---|---|---|
| | | | Liver | Kidney | Heart | Spleen |
| Healthy control (10% sucrose) | 40.83±11.80 | 0.1±3.83 | 2.95±0.27 | 0.55±0.04 | 0.42±0.03 | 0.415±0.02 |
| Diabetic (10% sucrose) | 20.83±5.56 | 0.06±0.01 | 3.23±0.35 | 0.79±0.07 | 0.54±0.13 | 0.61±0.14 |
| Healthy control (10% fructose) | 30.5±9.37 | 0.07±0.02 | 2.68±0.2 | 0.71±0.07 | 0.54±0.02 | 0.55±0.02 |
| Diabetic (10% fructose) | 32±10.2 | 0.08±0.02 | 3.26±0.51 | 0.77±0.09 | 0.58±0.06 | 0.54±0.04 |
| Healthy control (10% sucrol) | 29.66±3.61 | 0.07±3.94 | 3.22±0.24 | 0.86±0.08 | 0.49±0.03 | 0.54±0.05 |
| Diabetic (10% sucrol) | 35.83±5.77 | 0.09±0.01 | 3.12±0.34 | 0.73±0.16 | 0.52±0.06 | 0.54±0.05 |
| L.S.D. % 1<br>L. S. D. % 5 | 13.11<br>9.73 | 0.02<br>0.01 | ---<br>0.38 | 0.13<br>0.10 | 0.05<br>0.04 | 0.11<br>0.80 |

Values are expressed as means ± SD, n = 6 rats.

$$\text{* Feed eficiency} = \frac{\text{weight gain (g)}}{\text{food intake (g)}}$$

Generally it was found that, there was non significant increase in the mean values of the relative liver weight between all the different group of rats. But, there were significant increase in relative organ weights of kidney and heart in either 10 % sucrose alloxan-diabetic diet or 10 % fructose alloxan-diabetic diet than did their corresponding controls.

On the other hand, the results of Group 6 showed that, all the organs relative weights were non significantly different (except mean value of the relative kidney weight), that was significantly decreased ($P < 0.01$) when compared with its control.

It could be observed from Table (2) that, the lowest value of serum glucose was noticed in the diabetic rats that received 10 % fructose (136.63 ± 3.27) following by 10% sucrol diabetic rats (139.2 ± 2.28). But the highest value of serum glucose was for diabetic rats that received 10 % sucrose (150 ± 3.27) as compared with non diabetic rats group.

These results are in agreement with those reported by Bantle et al. (1983), where in their study, either 42 g of sucrose, fructose, wheat or potato strach, were in corporated into breakfast, together with 30 g rice strach, and found little difference in subsequent blood glucose levels. Similar results have been shown for patients with non-insulin-

**Table (2): Effect of dietary different sweeteners on serum glucose and lipid profiles.**

| Groups | Glucose mg/dL | Total lipid g/L | total chol. mg/dL | Triacylglycerol mg/dL | HDL-chol. mg/dL | VLDL-chol mg/dL | LDL-chol. mg/dL |
|---|---|---|---|---|---|---|---|
| Healthy control (10% sucrose) | 98.03±6.18 | 2.03±0.07 | 113.34±5.14 | 161.83±8.70 | 61.38±4 | 32.43±1.74 | 19.52±3.66 |
| Diabetic (10% sucrose) | 150±3.27 | 2.55±0.21 | 105.62±4.31 | 152.3±15 | 57.7±4.14 | 30.57±3.04 | 17.28±3.61 |
| Healthy control (10% fructose) | 105.68±2.65 | 2±0.21 | 103.16±3.36 | 157.8±13.8 | 51.95±1.1 | 31.64±2.66 | 19.5±1.58 |
| Diabetic (10% fructose) | 136.6±3.27 | 2.26±0.71 | 127.33±5.4 | 209.8±15.6 | 60.5±2.2 | 42.03±3.09 | 24.77±2.9 |
| Healthy control (10% sucrol) | 104.67±3.49 | 1.84±0.05 | 95.50±4.5 | 100±4.38 | 55.14±3.09 | 20.07±0.87 | 20.29±2.7 |
| Diabetic (10% sucrol) | 139.3±2.28 | 1.83±0.13 | 91.61±5.03 | 102.1±3.06 | 43.58±4.67 | 20.59±0.5 | 27.43±1.57 |
| L.S.D. % 1<br>L. S. D. % 5 | 5.99<br>4.45 | 0.22<br>0.16 | 7.45<br>5.53 | 17.95<br>13.33 | 5.22<br>3.87 | 3.45<br>2.63 | 4.4<br>3.26 |

Values are expressed as means ± SD, n = 6 rats

dependent diabetics (NIDDM) (Slama et al., 1984; Erkelens et al., 1985; Vorster et al., 1987; Abraira and Derler, 1988). In the present study serum glucose decrease in diabetic rats that received either 10 % fructose or 10 % sucrol than did the corresponding 10 % sucrose, may be due to the nature of sorbitol and mannitol that are slowly and poorly absorbed from the gut; and that 70-80 % can be recovered from the ileum. Little mannitol is metabolised (Nasrallah and Iber, 1969), but sorbitol is dehydrogenated by sorbitol dehydrogenase to fructose. All enter the liver cell independent of insulin, dietary sorbitol does not appear in plasma, and even when infused directly (Gabbay, 1973).

Al Zbeta and Michal (1996) reported that sorbitol has been widely accepted as sugar substitute for the use in well managed diabetic diet. While Bioresco et al. (1992) reported that glycaemic control in diabetics may be improved by regular daily intake of 50-100 g fructose. Xylitol, sorbitol and maltitol are accepted food additives which may replace sucrose as sweeteners.

Data present in Table (2) showed a significant increase of total cholesterol, HDL-C, triacylglycerol and VLDL in diabetic group that received 10 % fructose as compared with other two diabetic groups ($P < 0.01$). The results are in agreement with these reported by Nikkila (1974) who found that, diet high in fructose may also increase serum triacylglycerol more than carbohydrate source, by increasing hepatic synthesis and release of triacylglycerol.

On the other hand, Mayes (1993) found that, high level fructose feeding significantly affects carbohydrates and lipid metabolism resulting in increased hepatic secretion of very low density lipoprotein (VLDL).

It can be seen from Table (2) that, the serum total cholesterol, triacylglycerol, HDL-C and VLDL-C were affected and significantly decreased ($P < 0.01$) by using 10 % sucrol in alloxan diabetic diet as compared with the other two alloxan-diabetic diets. These results are closely related with those reported by Ellwood et al. (1999) who reported that, diet containing 20 % sugar alcohol decreased levels of plasma triacylglycerol and cholesterol.

Table (3) showed that a significant increase ($P < 0.01$) in the activity of both ALT and AST levels in diabetic rats that received either 10 % sucrose or 10 % fructose relative to the corresponding 10 % sucrol diabetes rats. These elevations are more specific indications for acute liver damage and hepatic dysfunction (Irwin and Staton, 1969).

Table (5): ... different sweeteners on serum activity of ALT and AST.

| Groups | ALT IU/L | AST IU/L |
|---|---|---|
| Healthy control (10% sucrose) | 11.33±1.63 | 44±4.05 |
| Diabetic (10% sucrose) | 28.5±2.81 | 74.33±1.9 |
| Healthy control (10% fructose) | 12.6±1.96 | 44.33±7.94 |
| Diabetic (10% fructose) | 29.3±1.03 | 71.33±2.7 |
| Healthy control (10% sucrol) | 19±1.67 | 57.66±11.96 |
| Diabetic (10% sucrol) | 13.66±0.81 | 52.66±7.0 |
| L.S.D. % 1<br>L. S. D. % 5 | 4.2<br>2.6 | 11.05<br>8.20 |

Values are expressed as means ± S. D, n = 6 rats

## CONCLUSIONS

It was concluded that the high glycemic index sucrose that is rapidly absorbed should be avoided in diabetic diet. If sweetness is needed, sugar alcohol (sucrol, . . .), is preferred as valuable component of low glycemic in diabetic diet plan.

## REFERENCES


Abraira, C. and Derler, J. (1988) : Large variations of sucrose in constant carbohydrate diets in type II diabetes. Am J. Med. 84, 193-200.

A.I.N. (1993) : American Institute of Nutrition. 1939-1951.

Al Zbeta and Michal (1996) : Natural and synthetic sweet substances. New York, London, P. 32-60.

Arcol, D. (1989) : Separation of high density lipoproteins and determination of cholesterol and phospholipids bound to these fractions : European, Heart. J. 15 : 121-124.

Bantle, J.P., Laine, D.C., Castle, G.W., Thomas, J.W., Hoogwerf, B.J. and Goetz, F.C. (1983) : Postprandial glucose and insulin responses to meals containing different carbohydrates in normal and diabetic subjects. N. Engl. J. Med. 309. 7-12.

ioresco, L.T.D, Binningen, L., Switz Erland (1992) : Sugar and sweeteners. 131-150.

llwood, K.C., Bhathena, S.J., Johannessen, J.N., Bryant, M.A., Donnell, M.W. (1999): Biomarkers used to assess the effect of dietary xylitol or sorbitol in the rat. Nutrition Research 19 : 11 – 1637-1648.

Erkelens, D.W., Stofkooper, A., Van den Bogaard, E. and Van der Snoek B.E. (1985) : Glycaemic effect of mono-di and polysaccharides in mixed meal in diabetic patients. Neth. J. Med. 28, 157-163.

Friedewald, W.T., Levy, R.J., Fredrickson, D.S. (1972) : Estimation of the concentration of low density lipoprotein cholesterol in plasma without use of preparative ultracentrifuge. Clin Chem. 18 : 499-509.

Gabbay, K.H. (1973) : The sorbitol pathway and the complications of diabetes. N. Engl. J. Med. 288, 831-836.

Harper, S. (1996) : Robert, K., Murray, D.K., Granner, P.A., Mayes, V.W. and Rodwell. Review of biochemistry 24 ed. Middle East Eedition.

Irwin, M.T. and Staton, A.J. (1969) : Dietary wheat starch and sucrose effect on levels of five enzymes in blood serum of young adults. Am. J. Clin. Nutr. 22 : 701-709.

Mayes, P.A. (1993) : Intermdiary metabolism of fructose. Am. J. Clin. Nutr. 58 Suppl 754S – 65S.

Moore, M.C., Davis, S.N., Mann, S.L. and Cherrington, A.D. (2001) : Acute fructose administration improves oral glucose tolerance in adults with type (2) diabetes. Diabetes Care 24 (11) : 1882-1887.

Nasrallah, S.M. and Iber, F.L. (1969) : Mannitol absorption and metabolism in man. Am. J. Med. Sci. 258 : 80-88.

Nikkila, E.A. (1974) : Influence of dietary fructose and sucrose on serum triglycerides in hypertriglyceridaemia and diabetes. In Sugar in Nutrition eds. Academic Press, New York, p. 439.

Reitman, S. and Frankel, S. (1957) : Kinetic determination of amino transferase activity. Am. J. Clin. Path.; 28-56.

Salminen, S., Salminen, E., Bridges, J.W. and Marks, V. (1985) : The effects of sorbitol on gastrointestinal flora in rats. Z. Ernahrungswiss, 25 : 91-95.

Schmit, J.M. (1964) : Colorimetric determination of total lipids using sulfophosphovanilic mixture. Lyno. Bio. Mericurx Company of France.

Sicard, P.T. and Leroy, P. (1983) : Mannitol, sorbitol and lycasin : properties and food applications. In : Developments in Sweeteners. Volume 2, pp. 1-25.

Slama, G., Haardt, M.J., Jean, Joseph, P. (1984) : Sucrose taken during mixed meal has no additional hyperglycaemic action over isocaloric amounts of starch in well controlled diabetics. Lancet II. 122-125.

Teuscher, A. and Richterich, P. (1971) : Enzymatic method of glucose. Schweiz Med. Wschr. 101 : 345 and 390.

Trinder, P. (1969) : Enzymatic method of triglycerides : Ann. Clin. Biochem. 6 : 24-27.

Vorster, H.H., Van Tonder, E., Kotze, J.P. and Walker, A.R.P. (1987) : Effects of graded sucrose additions on taste preference acceptability glycenic index, and insulin response to butter beam. Am. J. Clin. Nutr. 45, 575-579.

Winer, B.J. (1971) : Statistic principle in experimental design. M.C. Craw-Hill, New York, NY.

Wronstadt RE and Schellenberger RS (1981) : Free sugars and sorbitol in fruits-a complilation from the literature. J. Ascoc. Anal. Chem. 64. 91.

Yoshihisa Sugita (1989) : Showed in answer-food additive book. Agimono Co. Inc. Cho. Xu Tokyo. Gaba.