

Full Length Research Paper

The effect of oral administration of honey and glucophage alone or their combination on the serum biochemical parameters of induced diabetic rats

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The effects of feeding honey on normal and alloxan induced diabetes rats treated and untreated were studied. In the experimental design, 25 rats were divided into five groups of five rats each, with Groups I and II serving as the normal and diabetic control, while Groups III, IV and V were the diabetic test groups administered with glucophage 500 mg/kg, glucophage in combination with honey (500 and 10 mg) and only honey (10 mg wet wt) per kilogram body weight respectively. All groups, (I - V) were fed with growers mash and water *ad libitum* for six weeks. The following parameters were assayed using standard methods; serum blood glucose, lipid profile, urea and creatinine. The differences observed in the serum level of HDL, triglycerides and total cholesterol in the test groups and diabetic control were statistically significantly ($p \geq 0.05$) compared to the normal control. The same was the case for low-density lipoprotein (LDL) serum level in the test groups which was statistically insignificant to the normal control while LDL serum level in diabetic control was significantly ($p \geq 0.05$) higher than the normal control. The difference in the LDL and total cholesterol level in the test groups were statistically significant to the diabetic control except cholesterol level of the Test III that was statistically insignificant to the diabetic control. High-density lipoprotein (HDL) and triglycerides in the test groups were statistically insignificant to the diabetic control. The blood glucose level in the combined therapy group (Test II) gave an acceptable range in both the fasting and 2 h postprandial compared to the diabetic and honey control group respectively. In conclusion, honey should be administered along with hypoglycemic agent in diabetic condition for use as alternative sweetener.

Key words: Diabetes, honey, glucophage.

INTRODUCTION

Sweeteners are ingredients that add sweetness to foods. There are two categories of sweeteners: nutritive and non-nutritive sweeteners. Example of nutritive sweetener is honey (Lynn, 2001).

Honey is sweet and viscous fluid produce by honey bees (genus *Apis*) and other insects from the nectar of flowers. Honey is also a popular sweetener and groups as a common house hold product used through out the world. Popularity comes not only of its being a natural sweetener but also many benefits proven or unproven associated with it. It has many medicinal uses described

in traditional medicine. Modern system of medicine is also finding the honey efficacious in various medicinal and surgical conditions (Frankel et al., 1998; Lubsy et al., 2003). Antimicrobial, antioxidant and wound healing properties of honey are being evaluated with successful outcome. Prevention and treatment of various infections due to wide variety of organisms and promoting surgical wound healing are some of the areas where honey is making its mark (Bansal et al., 2005). Obi et al. (1994) reported 5% v/v concentration of honey decreases the duration of diarrhoe in cases of bacterial gastroenteritis. Honey lowers glycaemic index in patients with diabetes (Chen et al., 2000; Ahmed et al., 2008).

In one of the clinical trials of Type I and II diabetes, the use of honey was associated with significantly lower

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glycaemic index than with glucose or sucrose in normal as well as Type I diabetes (Al-Walli, 2004). Type II diabetes had values similar to honey. Honey compared with dextrose caused a significantly lower rise in plasma glucose levels in diabetes subjects. It also cause reduction of blood lipids, homocystein levels and protein levels in normal and hyperlipidaemic subjects (Al-Walli, 2004). The active ingredient is honey is fructose. Fructose generates a small hyperglycaemic effect as it is absorbed slowly by our body as opposed to either sucrose or glucose (Brand, 2003).

Diabetes is a metabolic disorder which is due to insulin resistance or deficiency (Shulaman, 2000). It is a complex disease characterized by grossly abnormal fuel usage where by glucose is over produce by the liver and underutilized by organs. It is the most common serious metabolic disease in the world. Type I is caused by auto immune destruction of the insulin-secreting beta cells in the pancreas, Type II diabetes, by contrast, has a different cause and it is the most prevalent while gestational diabetes occurs during pregnancy. Diabetes and its associated complication have affected about 200 million people world wide representing 6% of the population. In diabetes condition, the blood sugar level is high, a condition referred to as hyperglycaemia. In this condition, the renal tubular glucose re absorption threshold is exceeded and glucose is excreted in urine, a process called glucosuria. The metabolic derangement is frequently associated with permanent and irreversible function and structural changes in the cell of the body, those of the vascular system being particularly susceptible. The changes lead to the development of well-defined clinical entities, when glucose concentration in the blood exceeds the capacity of the renal tubules to reabsorb, its forms a glomerular filtrate, glucosuria occurs. Glucose increases the osmolality of the glomerular filtrate and thus prevents the reabsorption of the water as its passes down the renal tubular system. This way, the volumes of urine is markedly increase and polyuria occurs. This in turns lead to lost of water and electrolyte which result in thirst and polydipsia (Stanley and Passmore, 1973; Allan et al., 2004). A striking feature of diabetes is the shift in fuel usage from carbohydrate to fats. Triacylglycerols are mobilized and ketone bodies are formed to an abnormal extent. Since ketones are acids, this high concentration put a strain on the buffering capacity of the blood and on the kidney which controls the PH by excreting excess H into the urine. H excretion is accompanied by Na, K, PO₄ and H₂O excretion causing severe dehydration leading to a decreased blood volume.

Diabetes complication may lead kidney failure thereby causing changes in urea and creatinine levels. Urea level become elevated in the blood principally due to increase in the breakdown of amino acids for energy since insulin uptake of glucose by cell is impaired (<http://www.cufpallief.com/test.htm>). Accelerated ketone

body formation can lead to acidosis, comma and death in untreated insulin-dependent diabetes.

Hyperlipidemias are common with patients with diabetes and further increase the risk of ischemic heart disease, especially in Type II diabetes. Detection and control of hyperlipidemia can reduce myocardial infraction, coronary deaths and overall mortality. In deed, even when low density lipoprotein (LDL) cholesterol concentration is normal or slightly raised in Type II diabetes (the major abnormalities being low HDL cholesterol and high triglycerides concentrations) the LDL particles may be qualitatively different and more atherogenic than those in non diabetic patients (Watkins, 2003).

AIMS AND OBJECTIVES

The research is aimed at evaluating the effect of administration of honey alone, glucophage alone or their combination for use as an alternative sweetener in the management of diabetes mellitus.

MATERIALS AND METHODS

Experimental design

Twenty five rats used in this investigation were albino rats (adult male) that were in-bred in the animal colony of the Department of Biochemistry, University of Maiduguri.

The weight of the rats ranges from 120 - 250 g. They were stabilized on standard laboratory feed (Grower's mash EGWA feed Jos, Nigeria) which contains 54% of carbohydrate, 13% fat, 10% protein, 20% fiber, 2% normal supplement and 1% vitamin and water.

They were kept in a well ventilated animal house and weighed weekly for four weeks. After which they were grouped into five groups of five (Making a total of 25 rats) as follows:

Group A: Normal control: Rats were not induced and untreated. They were given normal feed and parameters from this group serve as a base live data (control).

Group B: Rats were induced with Alloxan monohydrated (0.2 ml/200 g body weight) and untreated, this serves as the diabetic control group and in addition were given normal feed /water *ad libitum*.

Group C: Rats were induced with Alloxan monohydrate (0.2 ml/200 g body weight) thereafter they were treated with Glucophage hydrochloride tablet B.P 500 mg/100 g body weight twice a day with urine sugar monitored, this group served as the test Group (I).

Group D: Rats were induced with Alloxan monohydrate (0.2 ml/200 g body weight) and then treated with glucophage (as described in group B) for one week then treated with 1 ml of honey which was administered for 1 week this represents test Group II.

Group E: Rats were induced with Alloxan monohydrate as described above and then treated with honey (1 ml/200 g body weight) for 1 week. (Honey control).

Table 1. Shows the effect of feeding honey on lipid profile in normal rats.

Parameters/Groups	Total cholesterol	HDL	LDL	Triglycerides
Normal control	2.06±0.15 ^a	1.86±0.21 ^a	0.36±0.1 ^a	0.96±0.5 ^a
Diabetic control	2.86±0.38 ^a	1.26±0.64 ^a	0.96±0.11 ^b	1.9±0.63 ^a
Test I	2.06±0.17 ^a	1.62±0.19 ^a	0.52±0.13 ^a	1.06±0.21 ^a
Test II	2.22±0.3 ^a	1.82±0.4 ^a	0.48±0.13 ^a	1.18±0.61 ^a
Test III	2.3±0.4 ^a	1.4±0.12 ^a	0.54±0.11 ^a	1.44±0.79 ^a

Values are mean ± SD, n = 5, Values with different superscript along a column vertically are statistically significant (p≤0.05).

Table 2. Serum glucose level in normal, diabetic controls and test groups.

Parameters/Groups	Fasting blood glucose (Mmol/l)	2 h Postprandial
Normal control	3.86±0.38 ^a	4.26±0.64 ^a
Diabetic control	11.57±2.22 ^b	16.45±3.11 ^b
Test I	5.28±1.33 ^b	6.26±1.00 ^b
Test II	6.22±1.03 ^b	7.82±1.04 ^b
Test III	8.44±1.66 ^b	11.05±2.11 ^b

Values are mean ± SD, n = 5, Values with different superscript along a column vertically are statistically significant (p≤0.05).

Method of intubation

The intubations were done using stomach tube. The rats were maintained on a daily administration of glucophage 500 mg/100 g body weight b.d. (twice a day) 1 ml of honey /100 g body weight was administered to the test group treated with honey.

Method of blood collection (Serum)

At the end of the experiment, the rats were sacrificed and the blood was collected in a plain container. The blood was allowed to clot and centrifuged in an ultra centrifuge at 3500 rpm to obtain the serum. The serum was used for analyzing cholesterol, HDL, LDL, Triglycerides and Blood glucose level.

Determination of serum cholesterol

Free and esterified cholesterol in the sample originates by means of the coupled reactions with a colored complex formation that was measured spectrophotometrically as described by the (National Cholesterol Program Expert Panel, 2001; Fossati and Prencipe, 1982).

Determination of high density of lipoprotein (HDL)

VLDL and LDL in the sample precipitate with phosphotungstate and magnesium ions. The supernatant contains HDL. The HDL cholesterol is then spectrophotometrically measured by means of the coupled reactions described by Bustein et al. (1980), Bucole et al. (1973) and National Cholesterol Program Expert Panel (2001).

Determination of blood glucose

The enzymatic method of glucose oxidase was used as described

by Trinder (1965) and urine sugar was estimated using the clinistex test strips (Burgett, 1974).

RESULTS AND DISCUSSION

Table 1 shows the result of total cholesterol HDL, LDL, and total triglycerides level before and after the administration of honey. A test of significant was carried out between the normal control against the diabetic control and within test groups. The serum level of total cholesterol was significantly higher (p≥0.05) than the normal control; the same pattern was also observed in the test groups. HDL serum level in diabetic control was insignificantly lower than normal control and the same was observed down the groups. Triglycerides and LDL in the diabetic control were significantly higher than the normal control, except the serum level of LDL in the diabetic control that was significantly (p≤0.05) higher than normal control. The level of total cholesterol in the Test I was significantly lower than the diabetic control, the same was observed in Test II expect Test III that was statistically insignificant to the diabetic control.

HDL serum level in the test groups was significantly (p≥0.05) higher than the diabetic control. LDL serum level in the test groups was statistically significantly (p≤0.05) to the diabetic control while triglycerides serum level in the test groups was statistically insignificant to the diabetic control.

In Table 2 the diabetic control which is the groups that have not received any treatment after diabetic induction, they have a high cholesterol level than those that

Table 3. The effect of administration of honey on ASAT, ALAT and total protein in treated and untreated diabetic rats.

Group	Parameter		
	ASAT	ALAT	Total protein
Normal control	437.7±5.8	132.7±25.0	97.2±1.0
Diabetic control	486.3±108.5	167.3±44.5	95.2±18.0
Test I	426.8±29.8	143.0±41.9	90.5±2.7
Test II	377.6±41.3	117.2±30.5	82.6±6.4
Test III	422.7±143.1	94.7±41.9	80.3±7.6

Table 4. Electrolytes, urea and creatinine in normal, treated and untreated alloxan induced diabetic rats.

Group	Parameter					
	Na ⁺	K ⁺	Cl ⁻	HCO ₃ ⁻	Urea	Creatinine
Normal control	147.2±1.3	4.7±0.4	92.8±1.3	23.0±2.1	5.5±0.7	60.4±4.7
Diabetic control	136.0±3.8	8.1±0.7	120.6±4.2	14.6±0.6	15.6±3.1	78.4±4.2
Test I	141.2±1.9	5.9±0.6	93.2±2.6	20.4±1.1	7.7±0.9	58.4±3.5
Test II	146.6±7.1	8.5±1.3	102.0±7.5	22.0±4.3	8.8±3.4	57.8±2.4
Test III	141.2±0.8	6.4±0.8	92.0±2.8	18.8±1.8	8.0±3.3	58.2±4.9

received treatment. In the test groups, the group that have received treatment only glucophage have lower cholesterol level compared to those that have received both glucophage and honey or those that received only honey. The HDL also shows that it is higher in the group that received honey alone or honey with glucophage. LDL is higher in the diabetic control than in the group that received treatment. While those that received only honey have the lowest LDL level. Triglycerides are higher in the diabetic group when compared to the test groups. While in the test groups, the group that received combination therapy with honey and glucophage have a higher value of triglycerides compared to those that received only honey or glucophage.

Table 2 shows the serum blood glucose level of in the test groups in comparison with the normal and diabetic control. The blood glucose of the diabetic control is significantly higher when compared to both the normal control and the all the test groups, both at fasting and 2 h postprandial. This is consistent with earlier reports by Modu et al. (2008). The group that was given administered only glucophage, had a near normal blood glucose level both at fasting and 2 h postprandial compared to diabetic and honey control (Test III). This effect might be attributed to the increased peripheral absorption of glucose by glucophage (Sfikakis, 1988). But the group that was administered glucocphage in combination with honey recorded a slightly higher glucose level both at the fasting and 2 h postprandial. Even though the increase is within the normal range. This shows that honey when used in combination with a hypoglyceamic drugs, can serve as an alternative sweetener (Daisy and Ezira, 2007). While the group that

served as the honey control, recorded much higher blood glucose concentration both at fasting as well as 2 h postprandial compared to the normal control and Test I and II respectively. This result revealed that, the use honey singly in diabetic condition will result into hyperglyceamia and its continuous use under such conditions might result into complications associated with diabetes mellitus.

In Table 3, ALAT level is found to be higher in the normal control than in the test groups, while the diabetic controls have the highest level of ASAT. The ALAT is higher in the normal than the test group. The diabetic controls also have higher value of ALAT than the test group. The diabetic controls have higher ALAT value than the other test groups but the group that received only honey have the lowest ALAT concentration, followed by the group that received both glucophage and honey.

The normal controls have higher concentration of total serum protein than the other groups. The diabetic control also has higher concentration of total protein compared to the other test groups. The group that received only honey has the lowest total protein level.

From Table 4, the normal control have higher Na and HCO₃ concentration than all the other groups, while creatinine level is higher in the normal control than the test group, but the creatinine on the other hand is higher in the diabetic control than in the test groups as well as the normal control.

The K level is higher in the diabetic control and those taking only honey, while it is lower in the normal control group.

The normal control have lowest urea level, while diabetic control have the highest urea level which is followed by

the group treated with only honey.

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