# EFFECT OF NATURAL HONEY ON BLOOD GLUCOSE LEVEL OF ALLOXAN INDUCED DIABETIC RATS

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**Abstract**

*During the period of July 2008 to June 2009, an experimental study was carried out in the Department of Pharmacology & Therapeutics of Sir Salimullah Medical College in collaboration with BCSIR to see the effect of natural honey on blood glucose level. 24 matured male Long Evans rats, (250-300 grams each) were used in this study. The animals were divided into 4 groups containing 6 rats each. Group A received laboratory diet and Group B received natural honey 5ml/kg daily for 21 days. Group C consisting of 6 rats, on which diabetes were induced by intraperitoneal Alloxan injection 100mg/kg body weight, received normal laboratory diet for 21 days. Group D, consisting of 6 diabetic rats, received honey 5ml/kg body weight daily for 21 days. At the end of three weeks, it was found that daily ingestion of honey for three weeks effectively reduced ($P<0.05$) blood glucose level in rats with alloxan-induced diabetes. Honey could not reduce ($P>0.05$) blood glucose in controlled rats that did not receive Alloxan treatment. It is thus apparent that honey may be a useful adjunct in the management of diabetes, while serving as a sweetener, especially if taken in moderate quantities.*

***Key words:*** *Natural honey, blood glucose, alloxan induced diabetes.*

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**Introduction:**

Diabetes is a chronic disease that is relatively common throughout the world. It is becoming the third human 'killer' following cancer, cardiovascular and cerebro-vascular disease. According to the WHO reports, more than 150 million people throughout the world suffered from diabetes in 2004, WHO estimate shows, globally the number of persons with diabetes will rise to 221 million by the year 2010, and to 300 million by 2025.Diabetes patients suffer a reduced amount of insulin secreted in response to any glucose introduced into their blood. Consequently they have a restricted food amounts and varieties. The restriction put on their food deprive them of many elements in their natural form. To replace sugar in their food and drinks, diabetes patients use synthetic sweeteners like aspartame, saccharin and other artificial and chemical sweeteners which have no food value but have byproducts of harmful toxic side effects. Pure natural honeys in low doses may be recommended as a source of carbohydrates and even as a sweetening agent in place of sucrose to the human patient suffering from diabetes mellitus. In a study, it was demonstrated that oral administration of pure small and large bee honey could not produce a significant increase in glucose level in normal and diabetic rabbit where as the adulterated honey significantly raised the blood glucose levels in normal and hyperglycemic rabbit even at the lower dosages[1], In another study the effect of honey on selected variables in Alloxan induced and fructose induced diabetic rats demonstrated that honey may be a useful adjunct in the management of diabetes [2]. The long-term effects of feeding honey

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compared with sucrose and a sugar-free diet in rats showed that HbA1c were reduced significantly in honey-fed compared with rats fed sucrose or a sugar free diet [3],

Honey is considered a valuable medicinal food in Bangladesh but in our country no study is available thus far in support of this content. The focus of the present investigation, therefore, was to find out the effect of honey on Alloxan induced diabetes rats and as well as the effect of honey on blood glucose level in normal healthy rats.

**Materials and Methods:**

***Material:*** Natural unprocessed honey was collected from 'Proshika' (an NGO center for human development).

***Animal and diet***: 24 matured male Long Evans rats (250-300 gram) were divided into 6 groups each were allowed 2 weeks acclimatization to laboratory environment and they were fed normal laboratory diet and allowed to drink water ad labitum.

Induction of diabetes in rats:

***Experimental protocol:*** In this experiment the effect of chronic administration of honey on blood glucose level in both normal and diabetic rats were studied. The experiment was divided into two parts: part-1, and part -2.

In Part 1 the effect of honey on blood glucose level of normal rats were studied. The animals in this part were grouped as Group A & Group B. In group A which served as control consisting of 6 animals received laboratory diet and distilled water daily for 21 days. Group B consisting of 6 animals were served as experimental group were given honey 5ml/ kg for 21 consecutive days. On the 22nd day the fasting blood glucose level of both the groups was estimated .Body weight of the rats were recorded before and after the treatment.

In Part 2 the effect of honey on blood glucose level of diabetic rats were studied. Animals in this part of experiment were grouped as Group C & Group D. This experiment carried out on 12 rats was treated with a single dose of Alloxan (100 mg/kg body weight) intraperitoneally. Rats were then rested for 3 days and Diabetes was confirmed in induced rats by testing fasting glucose levels.

Group C served as control consisting of 6 diabetic rats received normal diet for 21 days and was then sacrificed. Group D- served as an experimental group consisting of 6 diabetic rats received honey 5ml/kg. for 21 days. On 22nd day the blood glucose level of the rats of the entire group was estimated. Body weight of the rats was recorded before and after the treatment.

**Results:**

In the part 1 experiment the effect of chronic administration of honey 5ml/kg for 21 days

on blood glucose level of normal rats were observed and it was found that honey did not produce any significant change in blood glucose level in comparison to vehicle (laboratory diet + distilled water fed) as shown in table-I.

**Table-I**

*Effect of chronic administration of honey on blood glucose level of normal rats*

| Group | No. of rats | Treatment | Fasting Blood Glucose Level mean±SE mmol/L | |
|---|---|---|---|---|
| A | 6 | Vehicle | 5.55 | ±0.23 |
| B | 6 | Honey | 5.53 | ±0.06 |

Effects of Alloxan on blood glucose level of normal rats were observed by a single intra peritoneal injection of Alloxan in a dose of 100 mg/kg body weight in rats .produce a significant rise of blood glucose level( $p<0.001$) in comparison to control as shown in table II.

**Table-II**

*Effect of Alloxan on blood glucose level of normal rats.*

| Group | No. of rats | Treatment | Fasting Blood Glucose Level mean±SE mmol/L | |
|---|---|---|---|---|
| A | 6 | Vehicle | 5.55 | ±1.64 |
| C | 6 | Alloxan | 13.13 | ±0.33 |

Mean blood glucose (fasting) level in Alloxan induced diabetic rats was 13.13±0.33 mmol/l whereas Mean blood glucose level in control rats was 5.55±0.23 mmol/l.

In the part II experiment the effect of chronic administration of honey on blood glucose level of Alloxan induced diabetic rats were estimated and this effect of chronic administration of honey on blood glucose level of Alloxan induced diabetic rats is shown in table III.

**Table-III**

*Effect of chronic administration of honey on blood glucose level of Alloxan induced diabetic rats*

| Group | No. of rats | Treatment | Fasting Blood Glucose Level mean±SE mmol/L |
|---|---|---|---|
| C | 6 | Vehicle | 13.13±0.33 |
| D | 6 | Honey | 12.13±0.24 |

Mean blood glucose level in Alloxan induced diabetic rats who received vehicle for 21days was 13.13±0.33 mmol/l. Mean blood glucose level in alloxan induced diabetic rats who received honey 5ml/kg for 21 days was 12.13±0.24 mmol/l. Honey produced a reduction in blood glucose level in comparison to untreated diabetic animals and the reduction was statistically significant ($p<0.05$).

*General observation:*

A general observation was also made to find out any differences in body weight and physical appearance The body weight of both the control and honey treated normal rats was found to be increased than their initial body weight and the physical appearance of both group was good.

The body weight of untreated diabetic rats was markedly reduced than their initial body weight. The animals were found drowsy calm and quiet. The body weight of honey treated diabetic rats was found to be insignificantly less than their initial body weight and their physical appearance markedly better in comparison to untreated diabetic rats. Mean food intake were significantly lower in honey-fed rats compared with those fed the standard diet.

**Discussion:**

In the present study, administration of a single dose of Alloxan (100 mg/ kg body weight) intraperitoneally in rats caused a highly significant increase in blood glucose level. The dose and route of administration of Alloxan was selected from previous observation [4]. Rachel Nimenibo-uadia *showed* that diabetes was induced in rats within 72 hour by the intraperitoneal administration of Alloxan dissolved in D/W (5%) in a dose of 100mg/kg body weight[4]. It was concluded that Alloxan is a potent hyperglycemic agent in rats. Thus the findings of the study are in well agreement with other study. The dose of honey used in this study was selected as the dose used by Akhtar and Khan, 1989[1]. Administration of honey 5ml/kg in normal rats for 21 consecutive days did not produce any significant change in blood glucose level. This finding is also in well agreement with Akhtar and Khan[1].

Honey was administered 5ml/kg orally for 21 days in Alloxan induced diabetic rats and the fasting blood sugar level were compared with the rats which received only laboratory diet after diabetic induction. The difference in corresponding blood sugar levels was statistically significant. Mean food intake were significantly lower in honey-fed rats compared with those fed the standard diet. This could be attributed to that consuming honey leads to a stable blood sugars for longer (rather than a rapid increase followed by a rapid decrease as is seen with sucrose) which, in turn, may lead to less hunger and less desire to eat. Reduction of food intake in honey-fed rats was not simply due to the different sugar composition of the diet, but may have been due, in part, to the other components of the honey. It is possible that the intake of honey may have had a physiological effect on the stomach**[5],** for example, there are reports that honey acts as if it contains acetylcholine and choline esters in it which could affect the gastric muscle. Other hormonal or neurotransmitter activities are also possible as a result of consuming honey, although nothing has been reported in the literature to support this**.**

Studies in this field are not numerous. Still it was demonstrated that honey may be a useful adjunct in the management of diabetes while serving as a sweetener especially in moderate quantities [2]. Other studies indicated that honey has good glucose tolerance in both diabetic and nondiabetic subjects[6-10,3] Therefore, the

observation made in the present study also revealed that honey may be a useful adjunct in the management of diabetes.

Another explanation of the lower blood sugar level seen in the honey-fed rats is the production of hydrogen peroxide by the honey, as in vitro research has shown hydrogen peroxide to be a strong insulin-mimetic agent.[11-13]. Levels of hydrogen peroxide production in honey vary depending on floral source, but were shown to be in the range of 0.5–3.5 mmol/l in high peroxide-producing honeys[14] and these levels were in agreement with the 1-3 mmol/l shown to induce tyrosine phosphorylation (an insulin-mimetic effect) in vitro[12-13]. It is possible; that hydrogen peroxide originating from the honey acts to facilitate the uptake of glucose from the blood (by stimulating insulin receptors on the cells), thereby preventing the surge in blood glucose and insulin that usually follows consumption of a high carbohydrate meal. But due to the limitation in the present study, the level of hydrogen peroxide could not be estimated. However, the above findings from other studies[11-13] support the observation made in this study.

Limited clinical studies have demonstrated that honey, sucrose and fructose do have differential effects on blood glucose levels [6,14,15]. In the two clinical studies[6,15] plasma glucose levels were significantly lower after 1–3 hours in both healthy and diabetic patients who had consumed honey (20-75 g) than in those who had consumed equivalent amounts of dextrose, sucrose or fructose. Similarly, sheep given daily IV infusions of honey (50-80 grams daily for 10-14 days) had decreased blood sugar levels compared with animals fed equivalent amounts of dextrose[16] .It is possible; therefore, that the ingestion of honey in the present study may have resulted in sustained lower plasma glucose levels. Of course, large differences in metabolism and activity occur between humans and rodents, and direct inferences cannot be drawn.

Honey has anti hyperglycemic effect in diabetic rats but it does not produce any significant change in blood glucose level of normal rats so it may be proposed that honey does not interfere with the normal homeostatic mechanism of the body. Further studies are suggested to validate these finding and to explain the anti diabetic effect of honey. The result of the animal experimentation may not to be truly extrapolated to human situation. It may be recommended that clinical trial and toxicity study is necessary before introduction of the honey in therapeutics.

**References:**


1. Akhtar MS, Khan MS. Glycaemic responses to three different honeys given to normal and alloxan-diabetic rabbits J Pak Med Assoc1989; 39(4): 107-13.
2. Fasanmade AA, Alabi OT. Differential effect of honey on selected variables in alloxan-induced and fructose-induced diabetic rats, Afr J Biomed Res 2008; 11: 191-6.
3. Chepulis L, Starkey N. The long-term effects of feeding honey compared with sucrose and a sugar-free diet on weight gain, lipid profiles, and DEXA measurements in rats. J Food Sci 2008; 73(1): H1–7.
4. Nimenibo-uadia *R.* Effect of aqueous extract of *Canavalia ensiformis* seeds on hyperlipidaemia and hyperketonaemia in alloxan-induced diabetic rats *Biokemistri 2003; 15(1): 7-15.*
5. Goldschmidt S, Hoppe HB. Seylers Z Physiol Chem 1995; 300: 158.
6. Samanta A, Burden AC, Jones GR. Plasma glucose responses to glucose, sucrose and honey in patients with diabetes mellitus: an analysis of glycaemic and peak incremental indices. Diabetic Med 1985; 2: 371-3.
7. Shambaugh P, Worthington V, Herbert JH. Differential effects of honey, sucrose, and fructose on blood sugar levels. J Mani Physiol 1990; 13: 322–5.
8. Al-Waili NS, Haq A. Effect of honey on antibody production against thymus-dependent and thymus-independent antigens in primary and secondary immune responses. J Med Food 2004; 7: 491-4.
9. Agrawal OP, Pachauri A, Yadav H, Urmila J, Goswamy HM, Chapperwal A, Bisen PS, Prasad GBKS. Subjects with impaired glucose tolerance exhibit a high degree of tolerance to honey. J Med Food 2007; 10: 473-8.
10. Chepulis LM. The effect of honey compared to sucrose, mixed sugars, and a sugar-free diet on weight gain in young rats. J Food Sci 2007; 72(3): S224–9.

11. Czech MP, Lawrence Jr, JC Lynne WS. Evidence for the involvement of sulfhydryl oxidation in the regulation of fat cell hexose transport by insulin. Proc Nat Acad Sci 1974; 71(10): 4174-7.

12. Hayes GR, Lockwood DH. Role of insulin phosphorylation in the insulinomimetic effects of hydrogen peroxide. Proc Nat Acad Sci 1987; 84: 8115-9.

13. Heffetz D, Bushkin I, Dror R, Zick Y. The insulinomimetic agents $H_2O_2$ and vanadate stimulate protein tyrosine phosphorylation in intact cells. J Biol Chem 1990; 265(5): 2896-902.

14. Al-Waili NS. Effects of daily consumption of honey solution on hematological indices and blood levels of minerals and enzymes in normal individuals. J Med Food 2003; 6(2): 135-40.

15. Al-Waili NS. Intravenous and intrapulmonary administration of honey solution to healthy sheep: effects on blood sugar, renal and liver function tests, bone marrow function, lipid profile, and carbon tetrachloride-induced liver injury. J Med Food 2003; 6: 231-47.

16. Al-Waili NS. Natural honey lowers plasma glucose, C-reactive protein, homocysteine, and blood lipids in healthy, diabetic, and hyperlipidemic subjects: comparison with dextrose and sucrose. J Med Food 2004; 7: 100-7.