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Original Article

# Effect of honey on the body weight of glibenclamide treated alloxan induced diabetic rats

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## ABSTRACT

**Aim/ Background:** One of the classical features of diabetes mellitus is weight loss which may become excessive in some cases. This basically results from muscle wasting due to increased catabolism of proteins. The commonly used anti-diabetic drug; glibenclamide may not effectively prevent the excessive weight loss experienced by some diabetics. This is the reason why some complain of even extreme weight loss while on medication. Thus addition of a natural product with the potential to prevent excessive weight loss and make diabetics appear healthy while on treatment may be necessary. The aim of the present study is to determine the effect of honey on the body weight of glibenclamide treated alloxan induced diabetic rats. **Methods:** This study was carried out between September and October, 2015. A total of 20 male wistar rats weighing 200-250g were grouped into four with 5 rats in each group. Diabetes mellitus was induced in all the rats by intraperitoneally injecting 2% alloxan solution as 200mg/kg body weight. Each rat was weighed before and after the experiment and recorded accordingly. The animals received respectively oral administration of the following: Group one; 5.0ml/kg/day of distilled water, Group two; 5.0ml/kg/day of 50% honey, Group three; 5.0ml/kg/day of 50% honey together with 0.6mg/kg/day of glibenclamide, Group 4; glibenclamide alone (0.6mg/kg/day). The animals were treated for 4weeks. **Results:** There was significant increase in the mean final weight of the honey treated group compared to their initial weight. Conversely, significant mean weight reduction was noted for rats treated with glibenclamide alone. However, when honey was added to glibenclamide treatment, the weight loss was minimized. **Conclusion:** The present study showed that addition of honey to glibenclamide in the treatment of alloxan diabetic rats significantly improved the body weight compared to when the drug was administered alone. The study suggests that glibenclamide has a limited capability to stimulate the already damaged beta cells to stimulate insulin. However, when given together with honey, its anti-oxidant components may have prevented excessive protein catabolism. There could also be possible honey-induced pancreatic beta cell regeneration.

KEY WORDS: Honey; Body weight; Glibenclamide; Diabetic.

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## INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by hyperglycaemia which is due to absolute or relative insulin deficiency. The rising prevalence of the disease in developing countries, coupled with its high cost of management (including food restrictions and medications) is of concern.

The condition is often associated with weight loss despite polyphagia. This is usually due to muscle wasting resulting from excessive protein catabolism in skeletal muscle [1] as a result of decreased uptake and utilization of glucose for energy. When the weight loss becomes excessive it may be embarrassing to the patient as he may appear emaciated. The commonly used anti-diabetic drug; glibenclamide may not effectively prevent the excessive weight loss experienced by some diabetics. This is the reason why some complain of even extreme weight loss while on medication. Thus addition of a natural product with the potential to prevent excessive weight loss and make diabetics appear healthy while on treatment may be necessary.

Renewed attention to alternative medicines and natural therapies has stimulated a new wave of research interest into nutrition-based interventions since they are cheaper and have lesser side effects [2].

Honey is a natural product that comprises predominantly fructose and glucose [3]. It also contains other bioactive constituents such as phenolic compounds, flavonoids, organic acids, carotenoid-derived compounds, nitric oxide metabolites, ascorbic acid, aromatic compounds, trace elements, vitamins, amino acids and proteins [4, 5]. Some these are antioxidant compounds (including ascorbic acid, monophenolics, flavonoids and polyphenolics) [6].

For decades, there has been interest in determining the effects of honey intake on glucose regulation disorders, and controversial results have been obtained. Some researchers recommend cautious consumption of honey by diabetic patients because it may cause a rise in glycated haemoglobin levels [7], while others have produced interesting results suggesting that honey may be a potential nutritional supplement for subjects with disorders of glucose homeostasis [8].

Fasanmade and Alabi [9] in their work indicated that addition of honey, as a supplement to the diet resulted in increase in body weight in rats. Bahrami et al [7] .,

investigated the effect of natural honey on body weight in type 2 diabetic patients and showed that 8-week consumption of natural honey can provide beneficial effect on body weight.

Alloxan when administered into the body damages the insulin secreting cells leading insulin-dependent diabetes mellitus [10]. The mechanism by which alloxan causes damage to the beta cells is not clear. However two mechanisms have been proposed which include rapid uptake of alloxan by these cells [11] and also formation of reactive oxygen species [12].

Some patients using glibenclamide often complain of weight loss. It is not clear whether this is due to a direct effect of the drug or related to the worsening effect of the disease itself. The mechanism of action of the drug glibenclamide is by binding to and inhibiting the ATP-sensitive potassium channels inhibitory regulatory subunit sulphonylurea receptor 1 in the pancreatic beta cells [13]. This results in membrane depolarization and opening of the calcium channels leading to an increase in intracellular calcium in the beta cells and subsequent release of insulin.

The aim of the present study is to determine the effect of honey on the body weight of glibenclamide treated alloxan induced diabetic rats.

## METHODS

This study was carried out between September and October, 2015 at the animal house of department of Human Physiology, university of Portharcourt. A total of 20 male wistar rats weighing 200-250g were obtained and divided into four groups of 5 rats each. The rats were acclimatized and maintained under laboratory conditions of temperature, humidity and light for two weeks. All animals were supplied with commercial pellet food and water *ad libitum*. The experiment was carried out according to the guidelines of animal experimentation at the University of Portharcourt.

Diabetes was induced in all the groups by intraperitoneally injecting 2% alloxan solution as 200mg/kg body weight [14] after an overnight fast.

Diabetes mellitus was confirmed in these animals by both hyperglycemia and clinical features.

Natural honey was obtained from local honey farmers in Etche local government area of Rivers state and diluted to 50%.

Each animal was weighed before the experiment and recorded accordingly as initial weight.

The animals were respectively administered the following;

Groups 1 received distilled water as 5.0ml/kg/day

Group 2 received 5.0ml/kg/day of 50% honey.

Group 3 received 5.0ml/kg/day of 50% honey together with 0.6mg/kg/day of glibenclamide.

Group 4 received glibenclamide alone (0.6mg/kg/day).

The animals were treated for a period of four weeks and final weights taken and recorded.

Statistical analysis was done using spss v 20. Data were expressed as mean ± SEM. Values were compared using analysis of variance (ANOVA) and differences in the values were considered statistically significant when $p<0.05$.

## RESULTS

Fig I showed the mean initial and final weights of the rats in different groups. There was significant increase in the mean final weight of the rats that received honey alone (group 2) compared to their initial weight ($p<0.05$). Conversely, significant mean weight reduction was noted for rats treated with glibenclamide alone (Fig II). However, when honey was added to glibenclamide, the weight loss was minimized.

## DISCUSSION

The mechanisms by which honey improves body weight are unclear. Perhaps, fructose which is its predominant constituent might have contributed to weight gain [15] as shown in fig.2 due to its hypoglycaemic effect and that its metabolism does not usually require insulin secretion [16].

Dietary fructose is known to activate glucokinase which is a key enzyme involved in the intracellular metabolism of glucose. It catalyzes the conversion of glucose to glucose-6-phosphate thereby decreasing blood glucose [17].

Since alloxan is known to selectively damage the pancreatic beta cells, then it will likely cause insulin dependent diabetes in the rats. Patients with type 1 diabetes will respond poorly to glibenclamide treatment and this probably explains the marked weight loss seen in group 4 (Fig.2). The drug alone has a limited capability to stimulate the already damaged

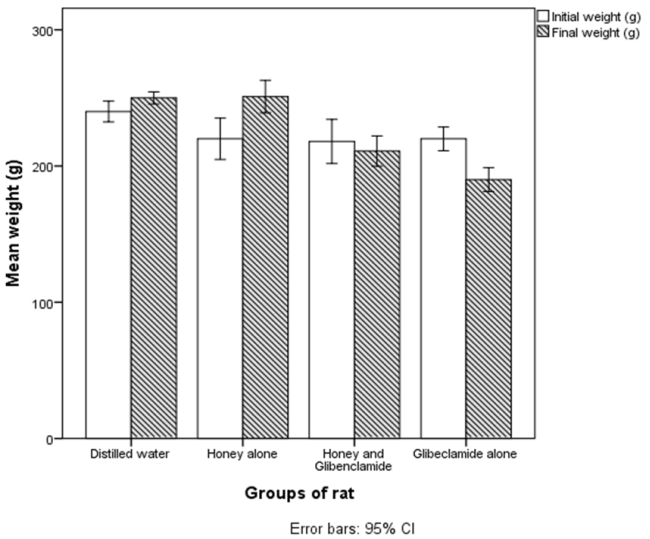


**Fig. I.** Comparison of the mean body weight of rats before and after experiment

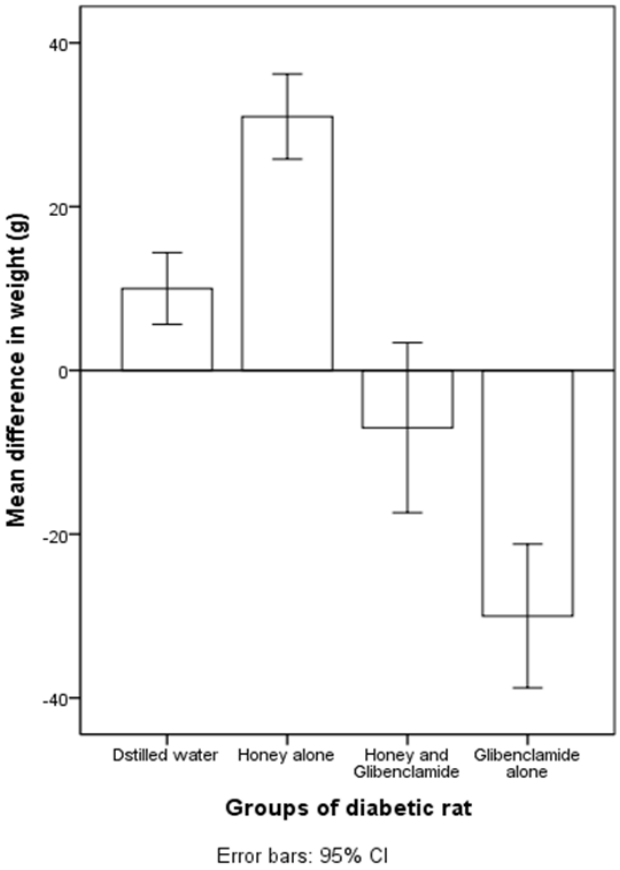


**Fig. II.** Mean difference in body weight of different groups of rat

beta cells to release insulin. This partly explains why it could not effectively reverse the weight loss associated with the disease. Weight loss may also probably be a direct effect of the drug.

The weight loss was only minimal when honey was added to the treatment (fig.2). This may be related to the anti-oxidant components of honey [6]. Anti-oxidants are known to have anti-catabolic properties, thus preventing excessive catabolism of proteins. Also the protein constituent of honey may replenish the proteins in the muscles. These together may lead to muscle recovery and therefore preventing excessive weight loss.

Furthermore, the hydrogen peroxide produced when honey is dissolved in water, helps in stimulating the remaining beta-cells to secrete insulin which suggest and further provides possible mechanism of the hypoglycaemic activity of honey in diabetes [18].

The honey treated group (Group 2) had significant weight gain. Honey has been known to cause regeneration of damaged cells by increasing prostaglandin E 2 and growth differentiation factor-9 [19] and its effect on the beta cell may enhance the repair of these cells thereby increasing its yield of insulin. The anti-oxidants in honey can also mop up the reactive oxygen species involved in alloxan destruction of beta cells, thereby preventing further toxicity to the cells. These can enhance insulin secretion and probably prevented excessive weight loss in the diabetic rats which received both glibenclamide and honey.

We therefore conclude that combining honey and glibenclamide in diabetic treatment may prevent excessive weight loss associated with diabetes in rats.

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