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Glycaemic Responses of Honeys in Normal and Alloxan-Induced Diabetic Rats

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ABSTRACT: This study investigated and compared the glycaemic rises following administration of various honey samples in rats. Five Nigerian honeys [Abakaliki honey (ABH), Calabar honey (CAH), Ezzamgbo honey (EZH), Lokoja honey (LOH), Okitipupa honey (OKH)] and one Malaysian honey (MAH) were administered to non-diabetic and alloxan-induced diabetic rats. Fasting blood glucose (FBG) concentrations were measured at 0, 30, 60 and 120 min. Glucose parameters including peak blood glucose, area under curve, percentage variation in blood glucose (BG) and percentage change in BG were estimated. At 30 min, all the honey samples significantly ($p < 0.05$) increased BG levels. Concerning BG levels at 60 or 120 min versus BG levels at 30 min, all honey samples except ABH produced significantly ($p < 0.05$) lower BG levels. LOH and MAH showed significantly ($p < 0.01$) lower BG levels at 120 min versus BG values at 0 min. The honey samples, except ABH and OKH, produced no significant rise in BG concentrations in diabetic rats. There was no significant difference in peak BG concentrations and AUC among the honey samples. Only CAH produced similar % change and % variation in BG as glibenclamide in diabetic rats. This study demonstrated that there were variations in glycaemic responses among honey samples collected in some states in Nigeria (Cross River, Ebonyi, Kogi and Ondo states). These differences in honey samples were more apparent in diabetic rats than in non-diabetic rats. These data suggest that diabetic patients may be more susceptible to detrimental effects of adulterated honey though a similar study in subjects with diabetes is warranted.

Keywords: Honey, Acute hyperglycaemia, Postprandial hyperglycaemia, Diabetes, Rats

Introduction

The pharmacotherapy of diabetes mellitus remains a challenge and is associated with many limitations (Raccah *et al.,* 2017) thus necessitating the need for re-evaluation of current management (Mazzi *et al.,* 2017; Swiaotoniowska *et al.,* 2019). Some diabetic treatment approaches requiring urgent re-examination include intervention with low glycaemic index diets, dietary fat restriction, targeting hyperglycaemia and oxidative stress concurrently (Erejuwa, 2012; Hardy *et al.,* 2020). The re-assessment of diabetes strategies becomes a

necessity considering the alarming number of diabetic patients who do not achieve adequate glycaemic control with the current antidiabetic regimen. Evidence implicates the role of excessive consumption of sugar-sweetened beverages in increased prevalence of metabolic diseases including insulin resistance, obesity and type 2 diabetes (Hu and Malik, 2010; Twarog *et al.,* 2020). This compelling evidence has resulted in a greater awareness on the benefits and potential deleterious effects of dietary carbohydrates on human health. Of particular interest are utilisation of low glycaemic index and low carbohydrate diets. Interventions involving these diets have the potential to suppress postprandial hyperglycaemia and improve glycaemic control (Feinman *et al.,* 2015).

Epidemiological evidence suggests that postprandial hyperglycaemia is an independent predictor of cardiovascular disease events not just in diabetic patients but also in non-diabetic population (O'Keefe and Bell, 2007). Postprandial hyperglycaemia may induce harmful effects on the cardiovascular system via several mechanisms including glucose-enhanced free radical generation and oxidative stress {Chong *et al.,* 2015), inflammation (Siklova *et al.,* 2015), impaired endothelial and vascular functions (Hoffman, 2015; Meza *et al*., 2019). Other mechanisms include increased cardiac ischaemia or reperfusion injury (Frantz *et al.,* 2005) and alteration of the coagulation system (Lemkes *et al.,* 2010). In healthy individuals, the various mechanisms that maintain glucose homeostasis (even following a high glycaemic load) are intact and functioning. One of these prominent mechanisms is the meal (glucose)-induced insulin response which enhances the peripheral uptake of glucose and suppresses hepatic gluconeogenesis and glycogenolysis. In a diabetic state, however, the glucose-stimulated insulin response is impaired or deficient partly due to β-cell dysfunction and/or insulin resistance (Halperin *et al.,* 2012). Hence, diabetes is frequently accompanied by elevated postprandial blood glucose (BG) concentrations.

Scientific findings implicating the role of postprandial hyperglycaemia in cardiovascular complications lend credence to the importance of preventing postprandial BG rise in diabetes. The glucose-lowering effect of honey has been demonstrated in rodents with diabetes (Erejuwa *et al.,* 2009) and in human subjects with diabetes (Abdulrhman *et al.,* 2013). Several factors such as botanical source, geographical origin and climatic conditions influence the composition of honey (Wang and Li, 2011) which may considerably affect the biological activities of honey. The issues of health beneficial effects of honeys being exclusive to certain types of honeys and generalization of the pharmacological effects of a particular honey sample to other honey samples of different botanical sources and/or geographical origins have been raised (Erejuwa, 2014), indicating the importance of further investigations on different kinds of honey.

Honey consists of primarily sugars - fructose and glucose. Therefore, consumption of honey may cause BG rise. This is of great concern considering that honey adulteration is a very common occurrence and global phenomenon. Ingestion of honey adulterated with sugars will probably pose a less health threat to non-diabetic subjects than to patients with diabetes due to their impaired glucose-stimulated insulin secretion. Studies showing that postprandial hyperglycaemia has a strong link with cardiovascular complications suggest that consumption of adulterated honey or honey samples having unusually low fructose to glucose ratio may be detrimental to health (Erejuwa, 2012). Recent evidence suggests that postprandial hyperglycaemia is a stronger risk factor of cardiovascular events than fasting plasma glucose in type 2 diabetic patients (Raz *et al.,* 2011). The latter evidence becomes even more relevant in view of the fact that ingestion of honey will elicit postprandial hyperglycaemia but not fasting hyperglycaemia. To our knowledge, there is no study to investigate these uncertainties. The aim of this study is to investigate and compare the glycaemic rises following administration of various kinds of honey in both normal and diabetic rats.

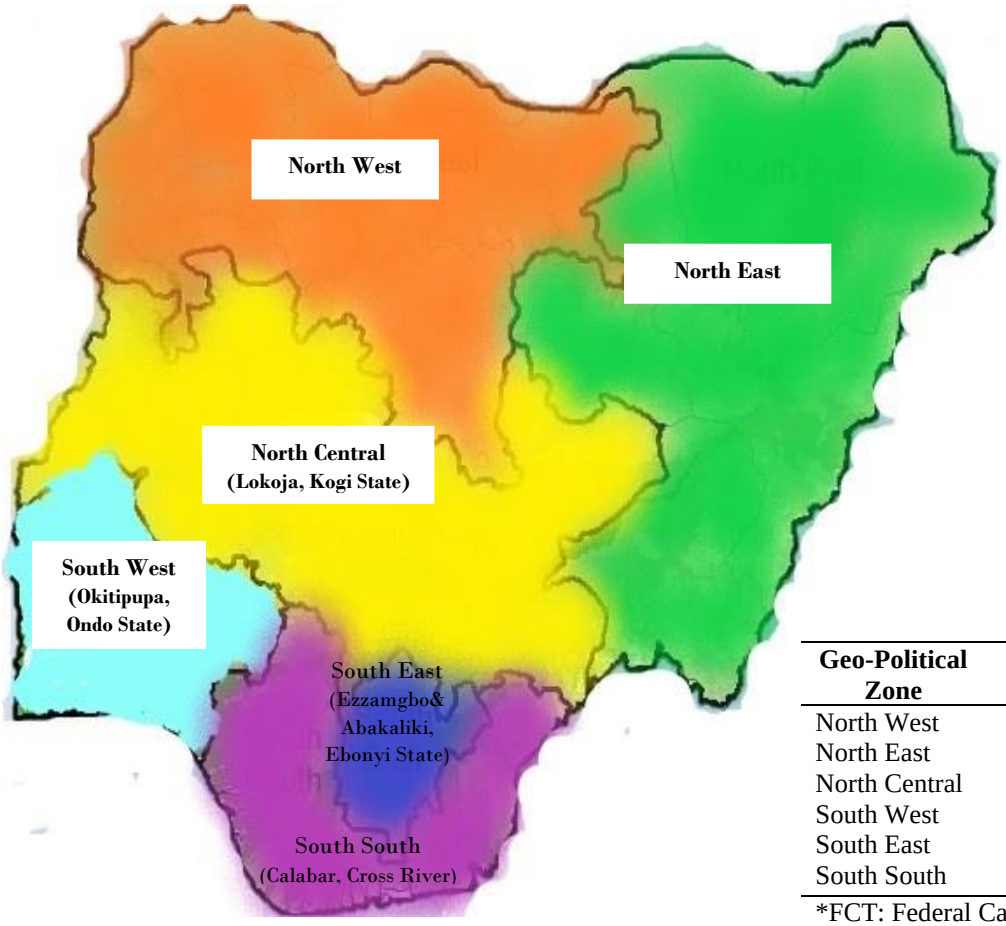
Materials and Methods

Materials: Alloxan, glucose, glibenclamide and dimethyl sulfoxide (DMSO) were purchased from Sigma-Aldrich, MO, USA. All other reagents used were of analytical grade.

Animals: A total of 113 Wistar rats (weighing 160 – 200 g) was used in the study. The rats were purchased from Enugu, Enugu State, Nigeria. The animals were housed individually in a cage. They were maintained in a well-ventilated animal room at 25-27ºC, humidity of 55 ± 5% and received 12 hours day: night cycle. The rats had free access to portable water and rat chow *ad libitum*. The research was approved by the University Research Ethics Committee of Ebonyi State University (EBSU/UREC/15/FCM/004). The animals were handled in accordance with institutional and international guidelines on the Use and Handling of experimental animals (United States National Institutes for Health, 1985).

Collection of honey samples: Six different samples of honey were used in this study. Five (5) honey samples were collected from different states of Nigeria to ensure a widespread in variability. The honey samples, which were wild and multifloral honeys, were named based on their place of collection: ABH (Abakaliki honey from

Abakaliki, Ebonyi State), CAH (Calabar honey from Calabar, Cross River State), EZH (Ezzamgbo honey from Ezzamgbo, Ebonyi State), LOH (Lokoja honey from Lokoja, Kogi State), OKH (Okitipupa honey from Okitipupa, Ondo State) and MAH (Malaysian honey from Malaysia). Two of the honeys (EZH and MAH) were collected from known sources to ensure authenticity of the honeys and minimise the chance of adulteration. EZH was purchased from Umuebe Farms Ltd., Ezzamgbo, Ebonyi State, Nigeria while MAH was supplied by FAMA (Federal Agricultural Marketing Authority), an agency under the Ministry of Agriculture, Malaysia. With the exception of the two honey samples, the remaining four honey samples were purchased with no regards to authenticity or quality. The honey samples were kept at room temperature before administration. Nigeria, divided into North and South, comprises six geo-political zones with each zone having varying number of states and distinct characteristic vegetations and weather conditions.



Geo-Political Zone	Number of states
North West	7
North East	6
North Central	6 and FCT*
South West	6
South East	5
South South	6

*FCT: Federal Capital Territory

Figure 1. Map of Nigeria showing the geopolitical distribution of the investigated honeys

Induction of diabetes mellitus: Diabetes mellitus was induced in overnight fasted male Wistar rats (160 – 200 g) via a one time intraperitoneal injection of alloxan (150 mg/kg body weight) dissolved in normal saline. Another group of fasted rats was administered normal saline without alloxan. Within the first 6 hours of alloxan injection, the rats were given glucose solution (20%) to prevent alloxan-induced hypoglycaemia. Forty eight (48) hours post-alloxan administration, rats which had elevated fasting BG concentrations ≥ 250 mg/dL were considered diabetic and included in the study.

Study design: The study design entailed two (2) studies. Study 1 involved administration of drinking water or honey samples to normal (non-diabetic) rats. Study 2, on the other hand, required treating alloxan-induced diabetic rats with drinking water or honey samples. The rats were randomly divided into seven groups (Study 1) and eight groups (Study 2). The rats were randomized in a manner that ensured the weight difference within and among the groups was comparable. Each group consisted of 6-7 rats. With the aid of an oral canula, portable water, honey or glibenclamide was administered to the rats once as follows:

Study 1:
Group 1: Non-diabetic rats administered 1 ml/kg body weight of portable water (CON)
Group 2: Non-diabetic rats administered 0.5 g/kg body weight of Abakaliki honey (ABH)
Group 3: Non-diabetic rats administered 0.5 g/kg body weight of Calabar honey (CAH)
Group 4: Non-diabetic rats administered 0.5 g/kg body weight of Ezzamgbo honey (EZH)
Group 5: Non-diabetic rats administered 0.5 g/kg body weight of Lokoja honey (LOH)
Group 6: Non-diabetic rats administered 0.5 g/kg body weight of Okitipupa honey (OKH)
Group 7: Non-diabetic rats administered 0.5 g/kg body weight of Malaysian honey (MAH)
Study 2
Group 1: Diabetic rats administered 1 ml/kg body weight of drinking water (CON)
Group 2: Diabetic rats administered 0.5 g/kg body weight of Abakaliki honey (ABH)
Group 3: Diabetic rats administered 0.5 g/kg body weight of Calabar honey (CAH)
Group 4: Diabetic rats administered 0.5 g/kg body weight of Ezzamgbo honey (EZH)
Group 5: Diabetic rats administered 0.5 g/kg body weight of Lokoja honey (LOH)
Group 6: Diabetic rats administered 0.5 g/kg body weight of Okitipupa honey (OKH)
Group 7: Diabetic rats administered 0.5 g/kg body weight of Malaysian honey (MAH)
Group 8: Diabetic rats administered 0.6 mg/kg body weight of glibenclamide (GLIB)
The honey samples and glibenclamide were dissolved in portable water and DMSO, respectively. They were prepared freshly each time they were administered. Before the commencement of treatment, fasting blood glucose (FBG) concentrations were measured using an Accu-Chek Active glucometer (Roche, Germany). The measured FBG concentrations at 0 min served as baseline values. Portable water, honey or glibenclamide was then administered to the rats based on their groups. Thereafter, the FBG concentrations were measured at 30, 60, and 120 min using the Accu-Chek Active glucometer.
Determination of peak blood glucose, area under curve, percentage variation in blood glucose and percentage change in blood glucose: The recorded FBG concentrations were used for the determination of peak blood glucose (PBG) concentrations, area under curve (AUC), % variation in BG and % change in BG.

The **PBG** concentration is the maximum BG concentration.

The **AUC** was calculated using the formula:

AUC = [0.25 × (BG0)] + [0.5 × (BG30)] + [0.75 × (BG60)] + [0.5 × (BG120)]

The percentage (%) variation in BG was calculated using the formula:

% variation in BG = [(BG30 + BG60 + BG120 – BG0) / BG0] x 100%

The percentage (%) change in BG was determined using the formula:

% change in BG = [(BG120 – BG0) / BG0] x 100%

where BG0, BG30, BG60 and BG120 are BG values at 0, 30, 60 and 120 min, respectively.
Statistical analysis: Data are expressed as mean ± SEM. The results were analyzed using SPSS version 18 (SPSS Inc., Chicago, IL). Each group consisted of at least 6 rats. Differences among the groups were assessed by one way analysis of variance (ANOVA) followed by Tukey's *post hoc* test.

Results

Effects of honey samples on blood glucose concentrations during the 120 minutes in normal and diabetic rats: Figure 2a shows the effects of honey samples on BG concentrations during the 120 min in normal rats. There was no significant difference in BG levels of control rats at 0, 30, 60 and 120 min. At 30 min, all honey samples significantly ($p < 0.05$) increased BG levels. Concerning BG levels at 60 or 120 min versus BG levels at 30 min, all honey samples but ABH produced significantly ($p < 0.05$) lower BG levels. LOH and MAH yielded significantly ($p < 0.01$) lower BG levels at 120 min compared with BG values at 0 min.

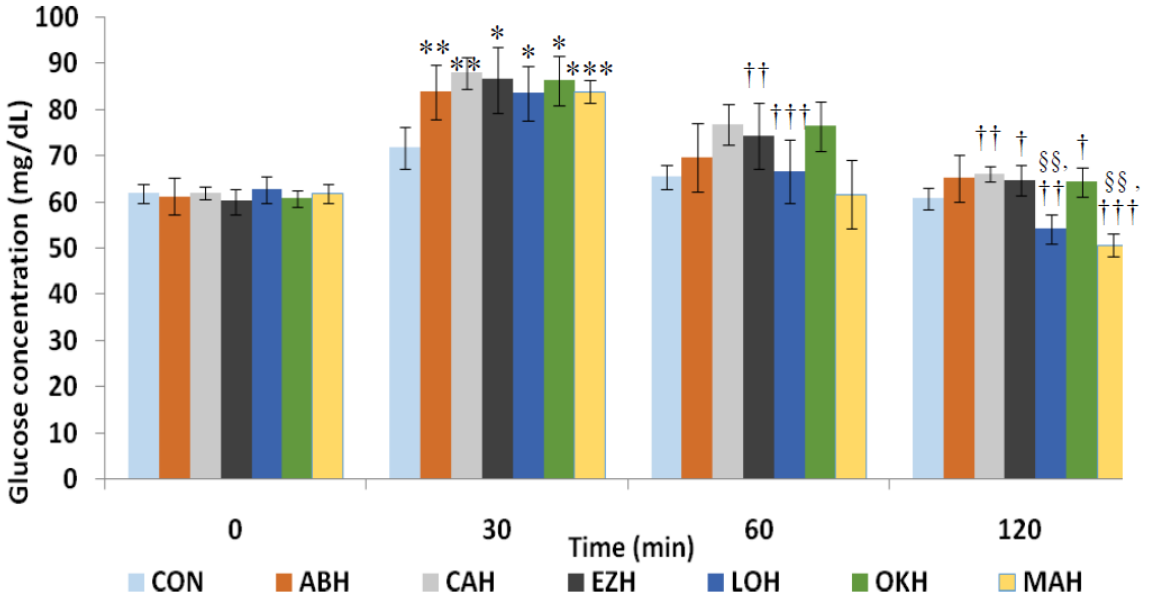


Figure 2a. Effect of honey on blood glucose (BG) concentration of normal rats.
Values are expressed as mean ± SEM, n = 6-7 per group. The groups consisted of normal rats administered portable water (CON), Abakaliki honey (ABH), Calabar honey (CAH), Ezzamgbo honey (EZH), Lokoja honey (LOH), Okitipupa honey (OKH) or Malaysian honey (MAH). A significant (* $p < 0.05$, ** $p < 0.01$ & *** $p < 0.001$) increase of BG value at 30 min compared with BG value at 0 min within the same group; A significant († $p < 0.05$, †† $p < 0.01$ & ††† $p < 0.001$) decrease of BG value at 60 or 120 min compared with BG value at 30 min within the same group; A significant (§§ $p < 0.01$) decrease of BG value at 120 min compared with BG value at 0 min within the same group. Data were analyzed with Repeated Measures ANOVA

Figure 2b shows the effects of honey samples on BG concentrations during the 120 min in diabetic rats. Administration of ABH and OKH caused a significant increase (** $p < 0.01$) in BG concentrations at 30, 60 and 120 min in diabetic rats. Administration of CAH produced significantly (†† $p < 0.01$) reduction in BG concentrations at 120 min versus at 60 min.

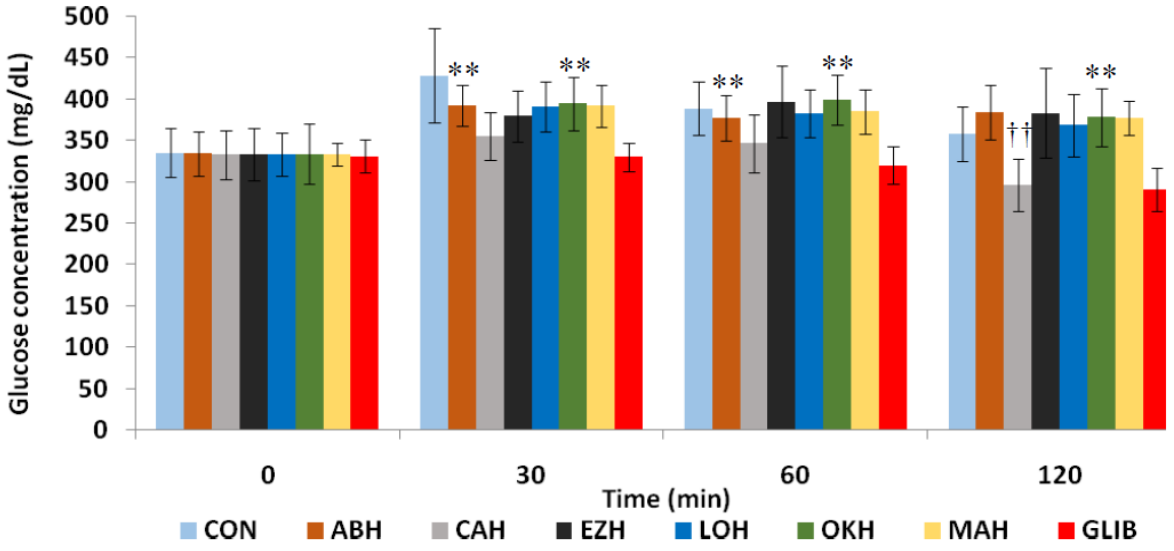


Figure 2b. Effect of honey on blood glucose (BG) concentration of diabetic rats.
Values are expressed as mean ± SEM, n = 6-7 per group. The diabetic rats were administered portable water (CON), Abakaliki honey (ABH), Calabar honey (CAH), Ezzamgbo honey (EZH), Lokoja honey (LOH), Okitipupa honey (OKH) or Malaysian honey (MAH). A significant increase (*$p < 0.05$ & **$p < 0.01$) compared with BG value at 0 min; A significant decrease (†† $p < 0.01$) compared with BG value at 60 min. Data were analyzed with Repeated Measures ANOVA.

Effect of honey on % variation in BG, % change in BG, PBG concentrations and AUC in non-diabetic and diabetic rats: The findings on the effects of honey samples on % variation in BG of diabetic rats are presented in Figure 3. Diabetic rats administered GLIB showed significantly ($p < 0.05$) lower % variation in BG compared to those administered portable water (CON). The % variation in BG in diabetic rats administered CAH was not significantly ($p > 0.05$) different from that of diabetic rats given GLIB. All the honey-administered diabetic groups (except CAH) yielded significantly ($p < 0.05$) higher % variation in BG compared with GLIB group. There was no significant ($p > 0.05$) difference in % variation in BG of non-diabetic rats administered honey samples (Table 1).

The results on the effects of honey samples on % change in BG of normal rats are presented in Table 1. MAH produced significantly ($p < 0.05$) lower % change in BG compared with CON. ABH, CAH, EZH or OKH caused a significant ($p < 0.01$) increase in % change in BG compared with LOH or MAH. In diabetic rats, most of the honey except CAH and LOH caused a significant increase in % change in BG compared with GLIB (Table 1). ABH and OKH produced a significant ($p < 0.05$) rise in % change in BG compared with CAH.

The data on the effects of honey samples on peak BG concentrations and AUC in non-diabetic and diabetic rats are presented in Table 1. There was no significant ($p > 0.05$) difference among the honey samples as well as compared with control in both non-diabetic and diabetic rats.

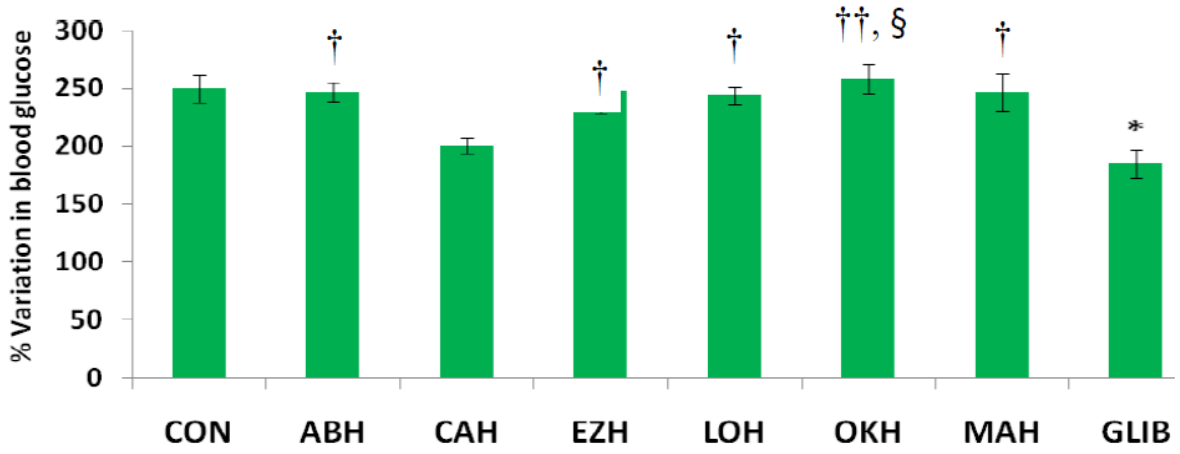


Figure 3. Effects of honey samples on % variation in BG in diabetic rats.

Values are expressed as mean ± SEM, n = 6-7 per group. The groups consisted of diabetic rats administered portable water (CON), glibenclamide (GLIB), Abakaliki honey (ABH), Calabar honey (CAH), Ezzamgbo honey (EZH), Lokoja honey (LOH), Okitipupa honey (OKH) and Malaysian honey (MAH). * A significant decrease ($p < 0.05$) when compared with CON; A significant increase († $p < 0.05$ or †† $p < 0.01$) compared with GLIB; § A significant increase ($p < 0.05$) compared with CAH

Table 1: Effect of honey on % variation in BG, % change in BG, PBG concentrations and AUC in non-diabetic and diabetic rats.

Groups	% Variation in BG	% Change in BG		PBG		AUC	
	Non-diabetic rats	Non-diabetic rats	Diabetic rats	Non-diabetic rats	Diabetic Rats	Non-diabetic rats	Diabetic rats
ON	221 ± 11	-1.6 ± 2.3	+6.9 ± 1.1	73.3 ± 4.0	435.8 ± 53.2	130.8 ± 4.7	768.3 ± 74.6
ABH	256 ± 6	+6.2 ± 3.9††	+15.3 ± 4.0†,§	83.8 ± 5.9	402.2 ± 30.6	142.0 ± 11.1	754.5 ± 55.2
CAH	273 ± 15	+6.7 ± 3.7††	-11.1 ± 3.4	87.8 ± 3.4	365.5 ± 32.5	150.0 ± 5.3	668.7 ± 62.3
EZH	273 ± 12	+7.5 ± 3.0††	+13.7 ± 10.2†	86.5 ± 7.1	416.6 ± 45.0	146.4 ± 10.7	762.0 ± 79.8
LOH	224 ± 12	-13.8 ± 2.4	+10.0 ± 4.1	83.5 ± 5.9	412.3 ± 30.5	134.5 ± 9.8	749.3 ± 58.0
OKH	274 ± 21	+5.8 ± 4.4††	+14.8 ± 3.8†,§	86.3 ± 5.4	407.3 ± 31.8	147.8 ± 7.8	769.0 ± 65.2
MAH	217 ± 13	-18.2 ± 1.7*	+13.4 ± 4.7†	83.8 ± 2.5	404.3 ± 22.8	129.0 ± 8.0	756.5 ± 43.1
GLIB			-12.1 ± 5.9		345.9 ± 17.4		632.8 ± 40.9

Table 1. Effect of honey on % variation in BG, % change in BG, PBG concentrations and AUC in non-diabetic and diabetic rats.

Values are expressed as mean ± SEM, n = 6-7 per group. The groups consisted of non-diabetic or diabetic rats administered portable water (CON), Abakaliki honey (ABH), Calabar honey (CAH), Ezzamgbo honey (EZH), Lokoja honey (LOH), Okitipupa honey (OKH), Malaysian honey (MAH) or glibenclamide (GLIB).

% Change in BG in non-diabetic rats: A significant increase (†† $p < 0.01$) compared with LOH or MAH; A significant decrease (* $p < 0.05$) compared with CON

% Change in BG in diabetic rats: A significant increase († $p < 0.05$) compared with GLIB; § A significant increase ($p < 0.05$) compared with CAH

Discussion

Several studies have compared the glycaemic rises of honey with those of other sugars such as sucrose, glucose and fructose. Generally, honey has been found to have a lower glycaemic index and/or cause lower postprandial rise than other sugars (Foster-Powell *et al.*, 2002; Abdulrhman *et al.*, 2013). Hence, this study compared the postprandial rises of various honey samples in non-diabetic and diabetic rats. At 120 minutes, MAH produced considerably lower BG concentration than did ABH or CAH in normal rats. At every time point, compared to CON or other honey samples, CAH elicited lower BG values in diabetic rats. The % change in BG resulting from the administration of ABH, CAH, EZH or OKH was significantly higher than that of LOH or MAH in normal rats. These findings clearly showed that there were marked differences among the investigated honey samples with respect to their acute glycaemic responses in non-diabetic rats. Similarly, in normal rats, only MAH supplementation exerted a significant reduction in % change in BG. This finding is of particular interest in view of previous observations. In previous studies that investigated the short- or long-term effects of MAH on glycaemia, no BG lowering effect in non-diabetic rats was found (Erejuwa *et al.*, 2009; Erejuwa *et al.*, 2011). It is worth mentioning that a particular effect observed in an acute study may not necessarily be detected in a chronic study. As reported by Ariefdjohan and colleagues, acute honey supplementation in rats enhanced intestinal absorption of calcium. This effect was not seen when the study duration was prolonged (Ariefdjohan *et al.*, 2008).

The data on the effects of honey administration on BG concentrations in normal rats over 120 minutes showed that all the honey samples caused significant elevations in BG at 30 minutes only. After 30 minutes, BG levels were markedly reduced towards the baseline values. These data may be interpreted to suggest or buttress the view that honey does not distinctly affect BG in a non-diabetic state. This phenomenon may be attributed to functional glucose-stimulated insulin response.

In diabetic rats, analysis of the effects of the various honey samples on BG concentrations over the period of 120 minutes revealed that the honey samples can be grouped into three categories. Among the six honey samples investigated, administration of ABH and OKH caused a significant rise in BG for the first 60 minutes and the entire 120 minutes, respectively. Supplementation of diabetic rats with EZH, LOH and MAH elicited no significant change in glycaemia throughout the 120 minutes period. On the other hand, CAH produced no significant change in BG for the first 60 minutes but then significantly reduced BG levels at 120 min compared

with 60 min. These findings evidently indicate the postprandial glycaemic responses of these honeys differ markedly especially in a diabetic state.

Even though ABH and OKH produced marked elevations in postprandial BG levels in diabetic rats, it is unclear if administration of these two honey samples will exert deleterious effects on the cardiovascular system. However, this may not occur for two reasons. First, the increase in postprandial hyperglycaemia following administration of ABH and OKH were not significantly different from that of CON. Second, oxidative stress is a main mechanism by which postprandial hyperglycaemia induces cardiovascular injury. Honey is a potent antioxidant which has been shown to ameliorate oxidative stress in several tissues and organs (Erejuwa *et al.,* 2012). Honey was also recently reported to mitigate against high-fat diet-induced postprandial oxidative stress (Erejuwa *et al.,* 2018). Therefore, the antioxidant effect of honey is likely to prevent oxidative stress (if any) that may result from honey-induced postprandial hyperglycaemia.

Due to paucity of data, it remains unknown if daily administration of ABH and OKH to diabetic rats will cause sustained hyperglycaemia. However, as explained earlier, available evidence suggests there is a discordance between the acute and chronic effects of honey (Ariefdjohan *et al.,* 2008). In view of the fact that postprandial hyperglycaemia is an acute response, therefore, postprandial increase in BG following ABH and OKH supplementation in diabetic rats does not suggest that these honeys would worsen hyperglycaemia or be devoid of any glucose-lowering effect. Hence, in the absence of data on the long-term effects of ABH and OKH on hyperglycaemia, it can neither be inferred that ABH and OKH would deteriorate hyperglycaemia nor lack glucose-lowering effects.

CAH, EZH, LOH and MAH are not likely to exert any injurious effects on the cardiovascular system because of their lack of postprandial rise in BG. Unlike ABH and OKH which elicited an acute rise in BG, CAH, EZH, LOH and MAH produced no such effect. EZH, LOH and MAH also did not elicit any significant reduction in postprandial hyperglycaemia. This may raise the question of whether the honey could exert glucose-lowering effect in diabetic rats. Currently, the potential glucose-lowering effect of CAH or LOH in diabetic rats is unknown due to lack of data. With regards to MAH, previous studies have demonstrated the glucose-lowering effect of this honey (Erejuwa *et al.,* 2009; Erejuwa *et al.,* 2010). In a more recent study, EZH has been reported to exert a glucose-lowering effect in diabetic rats (Erejuwa *et al.,* 2016). Despite the fact that acute administration of EZH, LOH and MAH did not reduce postprandial hyperglycaemia in diabetic rats, there is evidence to show that long-term supplementation with two of the investigated honeys (EZH and MAH) exerted glucose-lowering effect. Taken together, these data suggest that research investigating the effect of honey on glycaemia or its glucose-lowering effect should not rely exclusively on data obtained from an acute study. Instead, an acute study should be accompanied by a long-term or chronic study in order to obtain a more definitive inference.

In non-diabetic rats, with respect to percentage variation in BG, peak BG concentrations and AUC for glucose, there was no significant difference among the honey samples. Likewise in diabetic rats, the peak BG concentrations and the AUC for glucose did not differ among the honey samples. Honey adulteration is of public concern (Erejuwa, 2012). As stated in the methodology, most of these honey samples were intentionally purchased at places where likelihoods of adulteration were deemed higher. In spite of this, all the honey samples have comparable peak BG concentrations and AUC for glucose. This may suggest that determinations of peak BG and AUC for glucose are less sensitive to detect differences among honey samples.

Administration of glibenclamide produced significant reduction of percentage variation in BG in diabetic rats. This agrees with the antidiabetic effect of glibenclamide. Of all the honey samples, only CAH caused similar suppression on the percentage variation in BG as glibenclamide. This implies that CAH was uniquely different from other honeys. The fact that OKH caused greater percentage variation in BG than did CAH in diabetic rats further lends credence to variation among the honey samples. Interestingly, the data on the percentage variation in BG in non-diabetic rats yielded no significant difference among the honey samples suggesting that a diabetic state is vital in detecting BG variations among honeys. In other words, studies that assess differences among honeys should not consider non-diabetic animals or human subjects alone but also include diabetic rodents or human subjects with diabetes mellitus.

Our findings are consistent with outcomes from previous studies which showed that different types of honey may induce different glycaemic responses but with only minimal changes in BG (Naznin *et al.,* 2017; Rajab *et al.,* 2017). We confirmed that unlike peak BG and AUC, differences in honey samples were manifested as increments in BG at 30, 60 or 120 minutes as well as their % variation and % change in BG. As reported for other natural products (such as *Moringa oleifera*) with bioactive constituents and other low glycaemic index diets (such as cowpeas, African yam beans and pigeon pea) (Maiyaki-Musa *et al.,* 2016; Ukozor *et al.,* 2016), honey administration elicited low postprandial glycaemic rises.

Conclusion

This study revealed the presence of variations in glycaemic responses among different types of honey samples collected from some states in Nigeria. The differences in glucose parameters were more apparent in the diabetic rats than in non-diabetic rats. This may suggest that beneficial or deleterious effects of honey on glucose metabolism are likely to be more noticeable in subjects with diabetes than in healthy subjects. Similar studies in human subjects with diabetes mellitus are needed.

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