Natural Honey Modulates Physiological Glycemic Response Compared to Simulated Honey and D-Glucose

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ABSTRACT: The present study is undertaken to find out the relative glycemic tolerance of natural honey compared with simulated honey and D-glucose using oral glucose tolerance tested up to 180 min. Twenty-six healthy human subjects with mean age of 28.6 ± 9.3 y were randomly divided into 3 groups, that is, natural honey consumers (NHC; $n = 13$), simulated honey consumers (AHC; $n = 6$), and D-glucose consumers (DGC; $n = 7$). After recording fasting blood glucose, the participants consumed either natural honey or simulated honey or D-glucose (1g/kg body weight). Subsequently, additional plasma glucose levels (PGLs) were recorded at 60, 120, and 180 min. At 60 min, DGC and AHC group members exhibited similar PGL elevation (that is, 52% and 47%, respectively) compared to NHC group with only 20% increment. On the other hand, after 180 min, 20% decrease in PGL was observed in the DGC group compared to 9.75% reduction in the NHC group. These observations are primarily in line with earlier studies. Results analyzed by one-way analysis of variance (ANOVA) showed significant differences between all 3 tested groups with *F*-statistic (19.96) and *P* value (< 0.005). Coefficient of variation of the NHC, AHC, and DGC groups were 14.8%, 20.2%, and 27.5%, respectively. Posthoc tests showed that glucose response was significantly lower in the NHC group at all time points ($P < 0.005$) compared to the AHC and DGC groups. In conclusion, natural honey stabilizes physiological glycemic response with rebound recovery of PGL.

Keywords: diabetes, glucose metabolism, glycemic index, nutraceutical, nutrition

Introduction

Reduction in the rate of carbohydrate absorption by means of a low glycemic index (GI) diet plays an important role in the prevention and management of various pathological conditions, including cardiovascular diseases, diabetes mellitus, and cancers (reviewed in Augustin and others [2002]). In metabolic and dietary trials, foods with low GI exhibit reduced glucose responses (Björck and others 1994; Kalergis and others 2005). The GI quantifies the blood glucose change after eating a certain food compared to the "standard" food, for example, D-glucose and sucrose (Wolever and others 2006). Dietary carbohydrates are digested and absorbed at different rates and to different extent in the human intestine. The process of digestion depends on the botanical source and physical form of food (Cummings and others 1997). Food hydrolysis rate and gastric emptying time determine the absorption rate of that particular food, which in turn, determines the extent and duration of the glucose rise after a meal (Augustin and others 2002). In addition, absorption of the particular food is also affected by composition and types of carbohydrate, phytochemicals, and acids present. Influence of these factors results in variations of blood glucose responses of different diet (Grimes and Goddard 1977; Thompson 1988; Vosloo and Davel 1991; Southgate 1995; Asp 1997; Vosloo 2005).

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Beside a regular dietary component, natural honey exhibits an array of health benefits (reviewed in Khan and others 2007). Major constituents of honey are D-glucose 28% to 36%, D-fructose 36% to 50%, sucrose 0.8% to 5.0%, and maltose 1.7% to 11.8% (White and others 1962). Natural honey has been classified as GI food (Samanta and others 1985). GI analyses of honey have been carried on nondiabetic, diabetic, and hyperlipidimic human subjects as well as on rats. GI studies indicated that honey has good glucose tolerance in both diabetic and nondiabetic subjects (Samanta and others 1985; Shambaugh and others 1990; Al-Waili 2004; Agrawal and others 2007; Chepulis 2007; Chepulis and Starkey 2008).

The present study was undertaken to find out the relative glycemic tolerance of natural honey using oral glucose tolerance (OGT) tested up to 180 min in healthy nondiabetic subjects. The glucose response was compared with D-glucose, as well as with simulated honey, that is, a mixture of 4 predominant sugars present in natural honey.

Material and Methods

Test food

In the present study, unprocessed multifloral natural honey (collected from Swat area in Pakistan) was used. The simulated honey contained D-glucose 33.5 g, D-fructose 40.5 g, sucrose 1.5 g, and maltose 7.5 g dissolved in 17 mL sterile deionized water; this solution represents the proportion of the 4 predominant sugars in natural honey samples (Cooper and others 2002).

Study subjects

Twenty-six healthy subjects (35.7% nonpregnant females and 64.2% males; mean age of 28.6 ± 9.3 y) were recruited from Univ.

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of Karachi. These subjects were nonsmokers, and did not consume any medications in the last 2 wk. Written consents were taken from all subjects. Subjects were randomly divided into 3 groups, that is, (1) natural honey consumers group (NHC; $n = 13$), (2) simulated honey consumers group (AHC; $n = 6$), and (3) D-glucose consumers group (DGC; $n = 7$).

Experiment

The day before test session, the study participants were required to refrain from unusual amounts of eating and exercise, consuming alcohol, and legume-based meal and were requested to consume at least 300 g of carbohydrate for the whole day. The night before a test session, the study participants ate a regular evening meal and then fasted for 10 to 12 h overnight. During the fasting period, they were allowed to drink only water. The next morning they reported to the research center in a fasting condition. At zero time, fasting blood glucose was noted.

Immediately, the participants were given either natural honey, or simulated honey, or D-glucose dissolved in 250 mL of water at the rate of 1g/kg body weight (depending on which group the subject has been recruited). The study participants were required to consume all of the honey or reference food served to them. The participants were then required to remain seated at the research center and refrain from eating and drinking during the next 3 h. Additional blood samples were taken at 60, 120, and 180 min after consumption of meals. The glucose concentrations in blood samples were determined by the strip method employing a glucometer (Roche Diagnostics Ltd., Mannheim, Germany).

Table 1—Plasma glucose levels (PGL) of subjects before and after consumption of natural honey (NHC), simulated honey (AHC), and D-glucose (DGC).

	Mean PGL expressed in mg/dL			
Group ID	Fasting	After 60 min.	After 120 min.	After 180 min.
NHC	80.0	96.4 (20.5%↑)	70.5 (11.8%↓)	72.2 (9.75%↓)
AHC	73.4	108.2 (47.4%↑)	73.6 (0.2%↑)	77.4 (5.4%↑)
DGC	80.3	122.3 (52.3%↑)	88.2 (9.8%↑)	64.3 (19.9%↓)

Percentage increase or decrease in PGLs indicated within parentheses; change in PGL is shown by arrows.

Statistical analysis

Results were presented as mean and standard deviation. Coefficient of variation (CV) and one-way ANOVA with Tukey's HSD and Games–Howell test were performed to measure statistical differences between the 3 treatments. All analyses were carried out by using SPSS version-12 (Aspire Software Intl., Ashburn, Va., U.S.A.) and Microsoft Excel (Microsoft Corp., Redmond, Wash., U.S.A.).

Results and Discussion

The present study was conducted to compare the relative glycemic tolerance of natural honey with simulated honey and D-glucose in oral glucose tolerance (OGT) tested up to 180 min in healthy nondiabetic subjects.

The cumulative mean base line fasting glucose level of all 3 groups (that is, natural honey consumers group, NHC; simulated honey consumers group, AHC; and D-glucose consumers group, DGC) was 77.9 mg/dL. Table I shows comparative PGL in fasting as well as at 60, 120, and 180 min after test meal consumption by the NHC, AHC, and DGC groups. D-glucose elevated PGL at 60 min (52%) and at 120 min (approximately 10%) and decreased PGL after 180 min (20%). Natural honey elevated PGL after 60 min (20%) and decreased it after 180 min (9.75%). Hence, PGL increment after natural honey consumption is approximately 2.5 times less compared to D-glucose and simulated honey. Interestingly, these data are, for the most part, consistent with previous studies on glycemic response of honey (Al-Waili 2004).

Figure 1 depicts change in PGL compared to zero time. For this purpose, changes in PGL compared to fasting values for each subject were computed followed by statistical analyses. Figure 1 clearly illustrates variations in PGL at 60, 120, and 180 min after test meals consumption. Application of one-way ANOVA showed significant differences between all 3 tested groups with F-statistic (19.96) and (P value < 0.005). Tukey's HSD test and Games–Howell test showed that NHC was significantly ($P < 0.005$) lowers plasma glucose. Combine all point times coefficient of variation NHC, AHC, and DGC groups were 14.8%, 20.2%, and 27.5% respectively. An interesting observation was noted at 180 min when the DGC group showed continued decline in PGL (mean value of 64.3 ± 7.9 mg/dL), whereas the NHC and AHC groups showed recovery with mean BGLs of 72.2 ± 5.1 and 77.4 ± 3.1 mg/dL, respectively.

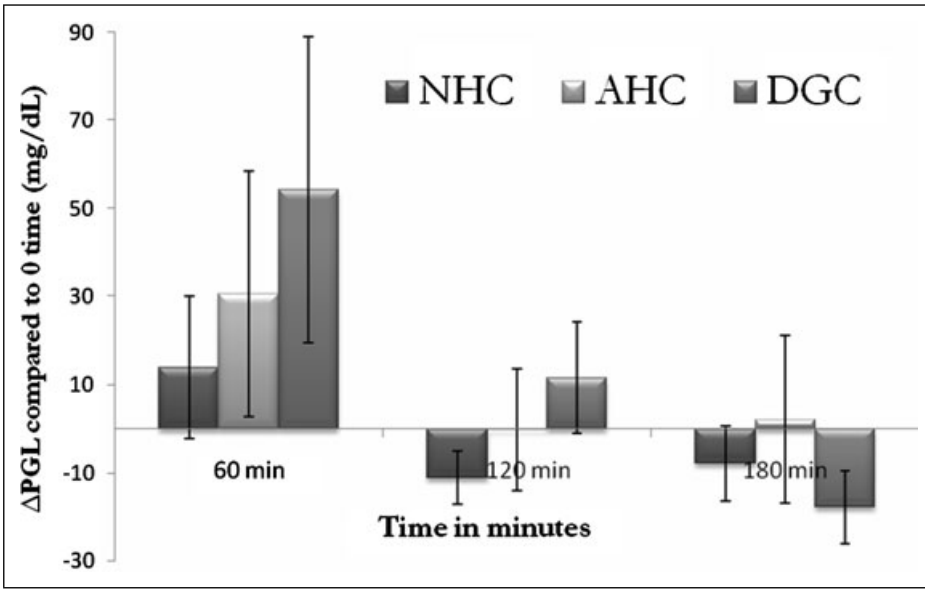

Figure 1—Changes in blood glucose concentration compared to zero time for each subject separately in all 3 studied groups, that is, natural honey consumers group (NHC; $n = 13$); simulated honey consumers group (AHC; $n = 6$), and D-glucose consumers group (DGC; $n = 7$). (A) Each bar represents mean ± SD values of 1 of the 3 groups studied, that is, NHC, AHC, and DGC.

Analyses of OGT responses (Table I; Figure 1) revealed that natural honey showed attenuated glycemic response as compared to D-glucose and simulated honey, as reported before (Samanta and others 1985; Shambaugh and others 1990; Al-Waili 2004; Agrawal and others 2007; Chepulis 2007; Chepulis and Starkey 2008). After 60 and 120 min, the DGC group showed the highest PGL followed by the NHC and AHC groups' BGL responses. After 180 min of meal consumption, the DGC group exhibited continued fall in BGL whereas the AHC and NHC groups showed rebound euglycemia. Nonetheless, the AHC group showed more recovery as compared to the NHC group. Calculation of coefficient of variation (CV) showed that the NHC group ($n = 13$) was the lowest (14.8%) compared to the other groups studied, indicating that natural honey is responsible for consistent, tight, and attenuated glycemic response with minimal variation among the relatively large, randomly studied human subjects. Moreover, as the natural honey mainly contains four sugars, i.e., D-glucose, D-fructose, maltose, and sucrose, the effect of natural honey on the postprandial PGLs was compared with that of D-glucose as well as with the mixture of major sugars constituents. For this purpose, a simulated honey sample was prepared that represents the proportions of 4 major sugars in natural honey (see Methods) (Cooper and others 2002).

The pattern of glycemic response observed after natural honey ingestion in this study, that is, neither overshoot nor steep decline in PGLs, might be due to multiple reasons that include following: (1) slowing down of the carbohydrate absorption due to various phytochemicals (for example, glycemic carbohydrates) in natural honey (Southgate 1995; Vosloo 2005); (2) fermentable (for example, D-fructose and D-glucose) and nonfermentable carbohydrates (glycoconjugates and oligosachharides) have been reported to modulate intermediary metabolism in the intestinal lumen (Wang and Gibson 1993; Kok and others 1998; Shamala and others 2000; Chow 2002); and (3) hydrogen peroxide (H_2O_2) present in honey might also take part in attenuation of glycemic response as it has been reported to be a strong insulin-mimetic agent (Czech and others 1974; Hayes and Lockwood 1987; Heffetz and others 1990).

In this study, we observed that the DGC group showed a steep fall in blood glucose near the level where one can experience the classical "hypoglycemic" symptoms; contrary to this observation, natural honey consumers with relatively large number of subjects did not touch the hypoglycemic level; rather, they showed rebound increase in blood glucose level, indicating that honey sugars metabolized differently as compared to glucose. Hence, the use of honey would be superior in avoiding hypoglycemia developed in diverse clinical situations. Isolation of glycemic response modulatory constituents of honey would be of great value for development as pharmaceutical agents, which could slow down the absorption of carbohydrates and eventually provide protection against harmful effects of postparendial hyperglycemia.

Conclusions

We have evaluated the glycemic response of natural honey in healthy nondiabetic subjects in comparison with D-glucose and simulated honey. The results demonstrate that natural honey decreased PGL with minimal variation at all time points. The NHC subjects exhibited rebound recovery of blood glucose after 180 min. Therefore, honey exerts its beneficial effects by regulating physiological blood glucose level.

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References

Agrawal OP, Pachauri A, Yadav H, Urmila J, Goswamy HM, Chapperwal A, Bisen PS, Prasad GBKS. 2007. Subjects with impaired glucose tolerance exhibit a high degree of tolerance to honey. J Med Food 10:473–8.

Al-Waili NS. 2004. 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 7:100–7.

Asp NG. 1997. Resistant starch—an update on its physiological effects. Adv Exp Med Biol 427:201–10.

Augustin LS, Franceschi S, Jenkins DJA, Kendall CWC, Vecchia CL. 2002. Glycemic index in chronic disease: a review. Eur J Clin Nutr 56:1049–71.

Björck I, Granfeldt Y, Liljeberg H, Tovar J, Asp NG. 1994. Food properties affecting the digestion and absorption of carbohydrates. Am J Clin Nutr 59:699–705.

Chepulis LM. 2007. The effect of honey compared to sucrose, mixed sugars, and a sugar-free diet on weight gain in young rats. J Food Sci 72(3):S224–9.

Chepulis L, Starkey N. 2008. 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 73(1):H1–7.

Chow J. 2002. Probiotics and prebiotics: a brief overview. J Ren Nutr 12:76–86.

Cooper RA, Molan PC, Harding KG. 2002. The sensitivity to honey of Gram-positive cocci of clinical significance isolated from wounds. J Appl Microbiol 93: 857–63.

Cummings JH, Roberfroid MB, Andersson H, Barth C, Ferro-Luzzi A, Ghoos Y, Gibney M, Hermonsen K, James WP, Korver O, Lairon D, Pascal G, Voragen AG. 1997. A new look at dietary carbohydrate: chemistry, physiology and health. Paris carbohydrate group. Eur J Clin Nutr 51:417–23.

Czech MP, Lawrence JJC, Lynne WS. 1974. Evidence for the involvement of sulfhydryl oxidation in the regulation of fat cell hexose transport by insulin. Proc Nat Acad Sci USA 71:4174–7.

Grimes DS, Goddard J. 1977. Gastric emptying of whole meal and white bread. Gut 18:725–9.

Hayes GR, Lockwood DH. 1987. Role of insulin receptor phosphorylation in the insulinomimetic effects of hydrogen peroxide. Proc Nat Acad Sci USA 84(22):8115–9.

Heffetz D, Bushkin I, Dror R, Zick Y. 1990. The insulinomimetic agents H_2O_2 and vanadate stimulate protein tyrosine phosphorylation in intact cells. J Biol Chem 265:2896–902.

Kalergis M, Grandpré ED, Andersons C. 2005. The role of the glycemic index in the prevention and management of diabetes: a review and discussion. Can J Diabetes 29:27–38.

Khan FR, Ul Abadin Z, Rauf N. 2007. Honey: nutritional and medicinal value. Int J Clin Pract 61(10):1705–7.

Kok NN, Morgan LM, Williams CM, Roberfroid MB, Thissen JP, Delzenne NM. 1998. Insulin, glucagon-like peptide 1, glucosedependent insulinotropic polypeptide and insulin-like growth factor I as putative mediators of the hypolipidemic effect of oligofructose in rats. J Nutr 128:1099–103.

Samanta A, Burden AC, Jones GR. 1985. Plasma glucose responses to glucose, sucrose and honey in patients with diabetes mellitus: an analysis of glycaemic and peak incremental indices. Diabetic Med 2:371–3.

Shamala TR, Shri JY, Saibaba P. 2000. Stimulatory effect of honey on multiplication of lactic acid bacteria under *in vitro* and *in vivo* conditions. Lett Appl Microbiol 30:453–5.

Shambaugh P, Worthington V, Herbert JH. 1990. Differential effects of honey, sucrose, and fructose on blood sugar levels. J Mani Physiol Ther 13:322–5.

Southgate DA. 1995. Digestion and metabolism of sugars. Am J Clin Nutr 62(Suppl 1):S203–10.

Thompson LU. 1988. Anti nutrients and blood glucose. Food Technol 42:123–32.

Vosloo MC. 2005. Some factors affecting the digestion of glycaemic carbohydrates and the blood glucose response. J Fam Ecol Cons Sci 331–9.

Vosloo MC, Davel EI. 1991. The effect of final temperature on the α-amylase activity, consistency and firmness of egg-starch pastes. J Diet Home Eco 19:82–6.

Wang X, Gibson GR. 1993. Effects of *in vitro* fermentation oligofructose and inulin by bacteria growing in the human large intestine. J Appl Bacteriol 75: 373–80.

White Jr. JW, Reithof ML, Subers MH, Kushnir I. 1962. Composition of American honeys. U.S. Dept. of Agriculture Technical Bulletin 1261. Washington, D.C.: U.S. Dept. of Agriculture.

Wolever TM, Ip B, Moghaddam E. 2006. Measuring glycaemic responses: duplicate fasting samples or duplicate measures of one fasting sample? Br J Nutr 96:799–802.