Arabic coffee increases the glycemic index but not insulinemic index of dates

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ABSTRACT

الأهداف: تحديد فيما لو أن المؤشر السكري والأنسولين للتمر يمكن أن يتغير بشرب القهوة العربية.

الطريقة: تم تطويع مشاركين أصحاء (5 إناث و5 ذكور) في هذه الدراسة. وتم إطعامهم تمر خلاص إما مع الماء أو مع القهوة العربية. وتم قياس استجابات جلوكوز وأنسولين بلازما الدم باستخدام الطريقة القياسية. وقورنت الاستجابات مع محلول الجلوكوز النقي المحتوي على نفس كمية النشويات المتاحة. وتم حساب المؤشر السكري والمؤشر الأنسولين بالطرق العيارية وعرضت النتائج كمتوسط حسابي ± الخطأ المعياري للمتوسطات الحسابية. ومن ثم مقارنة استجابات الجلوكوز والأنسولين باستخدام تحليل التباين المتكرر.

النتائج: بلغ المؤشر السكري للتمر 55 ± 6 وهذه القيمة قد ارتفعت إلى 63 ± 5 للتمر مع القهوة العربية، ولكن هذا الارتفاع لم يكن ذات دلالة إحصائية (p= 0.08). ومن ناحية أخرى، لم يتم ملاحظة أي اختلاف ذات دلالة احصائية بين المؤشر الأنسولين للتمر وللتمر مع القهوة العربية (p = 1.00).

خاتمة: سبب شرب القهوة العربية مع تناول التمر ارتفاع طفيف في استجابة جلوكوز الدم مقارنة بتناول التمر مع الماء فقط، في حين أن مستويات أنسولين الدم لم تتأثر بذلك. إن ارتفاع مستوى جلوكوز الدم للتمر في وجود القهوة يشير إلى أن هذه العادة قد تكون ضارة.

Objectives: To determine whether the glycemic index (GI) and insulinemic index (II) of dates could be altered by Arabic coffee consumption.

Methods: This randomized cross-over study was conducted at the Department of Nutritional Sciences, Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom from November 2009 to February 2010. Healthy subjects (5 males, 5 females) were recruited to the study. They were fed Khulas dates either with water, or with Arabic coffee. Plasma glucose and insulin responses were measured using standardized methods. Responses were compared with a pure glucose solution matched for available carbohydrate. The GI and II were calculated using standardized methods, and results were presented as means and standard error of mean. Glucose and insulin responses were compared using repeated measures analysis of variance.

Results: The GI of dates was 55 ± 6, which increased to 63 ± 5 for dates consumed with Arabic coffee (p=0.08). No significant difference was observed between the II for dates, and the II of dates consumed with Arabic coffee (p=1.00).

Conclusion: Arabic coffee consumption modestly increased the plasma glucose response of dates compared to that of dates consumed with water. Insulin levels were not significantly affected. The modestly higher glycemic response to dates in the presence of Arabic coffee indicates that this custom may be considered detrimental to health.

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The relationship between coffee consumption and the risk of developing type 2 diabetes mellitus (T2DM) has been studied in short-term randomized controlled trials and epidemiologic studies.[1-3] These studies have shown that high consumption of coffee beverage is associated with better glucose tolerance, and a substantially lower risk of T2DM.[1,3] This may in part, be related to coffee phenolic constituents where coffee is considered the major source of chlorogenic acids (CGA) in the human diet.[4,5] The CGA and other phenolic compounds in coffee may inhibit glucose absorption via interference with glucose transporters.[3,6,7] Also, CGAs have been shown to affect glucose metabolism by increasing insulin sensitivity.[4,5] Nevertheless, ingestion of coffee has also been shown to increase the area under the glucose and insulin curves, and to reduce insulin sensitivity,[8-10] in response to high and low glycemic index (GI) meals. This effect was associated with the presence of caffeine in the coffee beverage, which has also been shown to have important physiological effects.[8,9] There is evidence that dietary habits and lifestyle play important roles in developing, or preventing chronic diseases, such as diabetes.[3,11] Saudi populations habitually enjoy consuming Arabic coffee, which is mainly made from Arabica coffee beans which are lightly roasted, and then mixed with cardamom.[12] Arabic coffee is traditionally served along with varieties of dates on a daily basis. The GI for different varieties of dates ranges from 46-57.[13-16] Interestingly, the first documentation of the GI for dates came from a Saudi Arabian variety known as Khulas, which had a GI of 57.[13] A later study showed that the GI of dates can be reduced to 36 when they are consumed with sour milk.[17] A typical adult Saudi may consume between 20 and 120 g of dates with 60-300 mL of Arabic coffee at one sitting. However, although the effects of consuming dates with sour milk are known, the metabolic impact of consuming dates with Arabic coffee has not been investigated previously. It is apparent from our knowledge of the constituents of coffee that both beneficial and detrimental outcome could occur in terms of glucose and insulin levels by consuming coffee. The effect of consuming dates and Arabic coffee has not been investigated before, and as this is a traditional dietary habit in the Arabian Gulf countries, we were interested on its effect on blood glucose. Therefore, this study aimed to investigate the glucose and insulin responses to the ingestion of an equivalent amount of 50 g of available carbohydrate from dates with water, and dates with Arabic coffee.

Methods.

Total phenol content determination. The standardized Folin-Ciocalteu method[18] was applied to determine the level of total phenols in Arabic coffee colorimetrically using the Folin-Ciocalteu's reagent (Sigma Chemical Company Ltd., Poole, UK). Coffee beverage was prepared by dissolving coffee particles (4 g) in 100 mL boiled Milli-Q water. Ten mL of coffee beverage was added to a screw-capped tube containing 8 mL of 1.2 M hydrochloric acid in 50% methanol/water. The samples were then placed in a water bath at 80°C for 3 hours. A reagent blank was made using Folin-Ciocalteu's reagent diluted 1 in 9. The calibration standards were made using epicatechin at a concentration range of 0.025 - 0.3 mg/mL, in which 100 µL of each of these solutions were also reacted with Folin-Ciocalteu's reagent. For analysis of the coffee samples, 100 µL was used and reacted with the diluted Folin-Ciocalteu's reagent. The colorimetric measurement was carried out at 720 nm.

Liquid chromatography-mass spectrometry (LC-MS) analysis. Arabic coffee (*Coffea Arabica*) was analyzed for CGA, other components with a similar structure to CGA, and also other phenolic compounds. Coffee particles (375 g) were dissolved into 20 mL Milli-Q boiling water and left to stand for 2 minutes. Then, 10 mL of this coffee solution was transferred to a test tube containing 0.5 mL of Carrez A and then vortex mixed. Carrez B reagent (0.5 mL) was added and the sample was vortex mixed, and then centrifuged at 4000xg for 20 minutes at 4°C. Peaks were obtained corresponding to the retention times of a number of phenols and chlorogenic acids. Their identity was confirmed from their fragmentation patterns of standard compounds found within the Arabic coffee.

The GI and II determination. Subjects. A randomized cross-over design carried out in accordance with the FAO/WHO guidelines for GI testing was used.[19] This study was conducted at the Department of Nutritional Sciences, Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom from November 2009 to February 2010. The study design received ethical approval from the University of Surrey Ethics Committee (EC/2009/95/FHMS) and approved in accordance with the Helsinki II declaration. Ten healthy volunteers (5 men and 5 women, aged 30.8± 2.8 years) were recruited from the post-graduate student and staff population at the University of Surrey by distribution of both e-mails and posters. All volunteers gave informed written consent. Weight, height, fasting blood glucose, and blood pressure were measured at baseline. The inclusion criteria were healthy men and women aged between 18-60 years old and free from medication with the exception of minor analgesics. Participants were excluded from the study

when they have had familial or personal history of psychiatric disorders, epilepsy, sleep disorders, diabetes, cardiovascular disease, or food allergies, taken any medication, or were pregnant women.

Food test. Khulas dates (*Phoenix dactylifera L.*) and Arabic coffee (*Coffea Arabica*) were prepared in a kitchen at the Clinical Investigation Unit (University of Surrey). A portion of dates (which contained 50 g of available carbohydrate) was served to subjects with water, or Arabic coffee (no sugar added) on 4 separate sessions. On a further 3 separate occasions, a solution containing 50 g pure glucose (Fisher Scientific, UK) was given. Volunteers were asked to eat the dates and consume the drink within 10 minutes.

Blood sample collection. Participants arrived at the Clinical Investigation Unit at the University of Surrey at 0830 hour each study day of testing after an overnight fast (10-12 hours). Blood samples were obtained by finger pricks using preset lancets (Accu-chek Softclix Pro., Brighton, East Sussex, UK) at fasting, and at 15, 30, 45, 60, 90, and 120 minutes after consuming the dates, dates with Arabic coffee (no added sugar), or standard glucose solution. Blood samples were collected into 300 µL plastic microvette tubes (SARSTED Ltd., Leicester, UK) coated with fluoride oxalate, and were immediately centrifuged at 3000×g for 10 minutes at 4°C. The resultant plasma was transferred into separate 300 µL plastic plain microvette tubes (SARSTED Ltd., Leicester, UK). The tubes were then frozen and kept in the freezer at -20°C until analysis (within 4 weeks).

Glucose measurement. The plasma glucose concentration was determined using an automatic analyser (YSI 2300 STAT plus, Yellow Springs, Analytical Technologies, YSI, UK). It was an enzymatic method applied to the enzyme glucose oxidase in aqueous solution to oxidize the glucose and produce hydrogen peroxide. The hydrogen peroxide was then oxidized, and the current product was proportional to the concentration of the glucose. Twenty-four samples were analyzed in each run along with 3 quality control (QC) samples. Within each run the coefficient of variation of the QC1 was 2.5%, QC2 - 3.6%, and QC 3 - 1.8 %. The incremental area under the glucose curve (iAUC) for the reference glucose drink, dates, and dates with Arabic coffee was calculated using the trapezoid rule. The GI values of dates and dates with Arabic coffee for each subject were calculated as follows:

GI of dates or dates with Arabic coffee = iAUC for dates or dates with Arabic coffee / iAUC for reference × 100

The GI value of dates with water and dates with Arabic coffee was calculated as the average value obtained for 10 subjects.

Insulin determination. Enzyme linked immunosorbent assay (ELISA) was employed for measuring plasma insulin concentrations. Samples were thawed at room temperature and then centrifuged at 3000xg for 5 minutes to remove insoluble debris. The QCs, standards (Invitron Ltd, Monmouth, UK), and samples (25 µL per each) were incubated with the labelled antibody solution (Invitron Ltd, Monmouth, UK) at 37°C for 2 hours, and unbound labelled antibodies were removed using the wash buffer (Invitron Ltd, Monmouth, UK) according to the manufacturer's instructions. The insulin was then measured using the microtiter plate luminometer (Luminescent plate reader Centro LB 960, Berthold, Germany). All readings obtained from the luminometer were multiplied by 6 to convert the units (mU/L) into pmol/L. Two QCs (low and high) were used, and their CVs were 6.6% (low) and 4.9% (high).

Statistical analysis. Results were checked for normality using the Kolmogorov-Smirnov test (K-S test) and expressed as a means ± one standard error of the mean (SEM). Two factors repeated measures analysis of variance (ANOVA) was used to analyze differences in the mean of glucose and insulin. In addition, a single factor repeated measures ANOVA was used, as well, to analyze differences in the iAUC for glucose and insulin (Statistical Package for Social Sciences version 16 for Windows [SPSS Inc, Chicago, IL, USA]). If a significant interaction was obtained following ANOVA, a Bonferroni step-wise post hoc test was performed to determine the location of the variance. All data were examined using a 2-tailed approach with a level of $p<0.05$ considered as significant.

Results.

Phenol analysis. The amount of total phenols in Arabic coffee was calculated to be 1.2 mmol epicatechin equivalents/L using the standard curve presented in **Figure 1**. **Figure 2** shows the compounds that were identified within the Arabic coffee sample. The LC-MS analysis showed that the Arabic coffee contained CGAs and caffeine. The most abundant derivative was a caffeoyl quinic acid. The highest peak was shown for 5-Caffeoyl quinic acid followed by 3-Caffeoyl quinic acid, Caffeoyl quinic acid, and Caffeine. However, *p*-coumaroyl quinic acid, feruloyl quinic acid, and dicaffeoyl quinic acid were also observed in relatively small amounts. Identification was based on their retention time compared to that of the standard, absorbance spectrum, and MS fragmentation pattern.

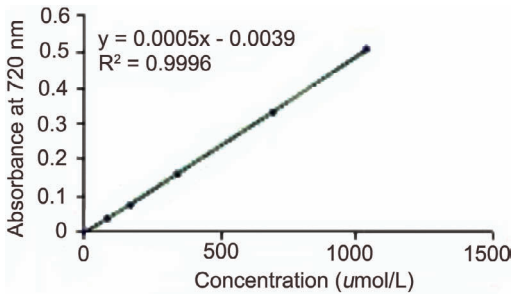

Figure 1 - Standard calibration curve for epicatechin.

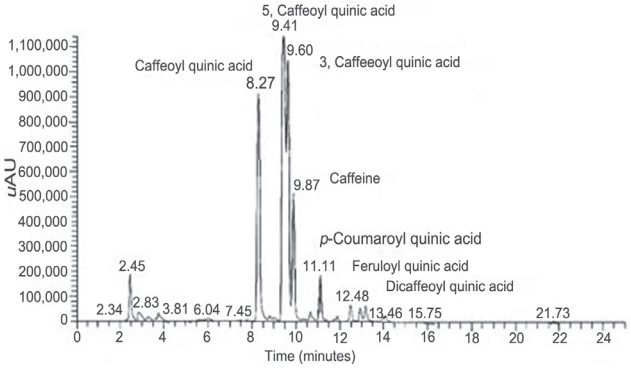

Figure 2 - Liquid chromatography-mass spectrometry analysis for Arabic coffee.

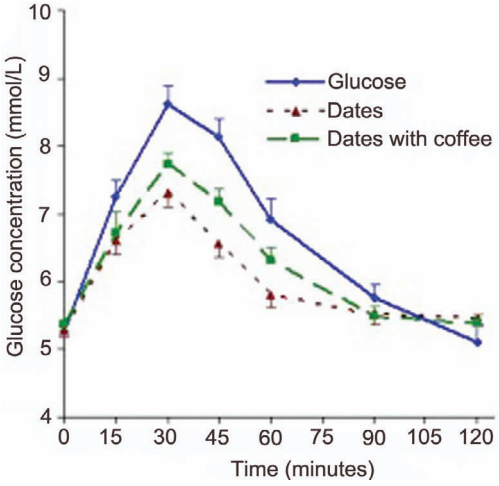

Figure 3 - Plasma glucose responses over 2 hours following consumption of reference glucose, dates, and dates with Arabic coffee. Results are presented as mean ± standard error of mean. Glycemic index was measured using standard procedures.[19] A 2-factor (treatment and time) repeated measures ANOVA was used to analyze differences in the means of glucose levels within the dates, dates with Arabic coffee, and standard glucose consumed. No significant differences were observed (p=0.08).

Determination of GI and II. Subjects' characteristics are shown in **Table 1**. They had an average age of 30 years, with normal weight, blood pressure, and fasting blood glucose levels. As shown in **Figure 3**, peak

Table 1 - Characteristics of subjects included in a study at the University of Surrey, Guildford, United Kingdom (N=10).

Characteristics	Mean ± SEM	Range
Age (year)	30.8 ± 2.8	18-48
Weight (kg)	75.0 ± 5.4	60-108
Height (m)	1.73 ± 0.02	1.60-1.87
Body mass index (kg/m^2)	24.0 ± 1.2	20.7-31.7
Diastolic blood pressure (mm Hg)	72.5 ± 3.2	54.0-86.5
Systolic blood pressure (mm Hg)	122.1 ± 2.8	105.6-135.0
Fasting blood glucose (mmol/L)	5.2 ± 0.1	4.5-5.8

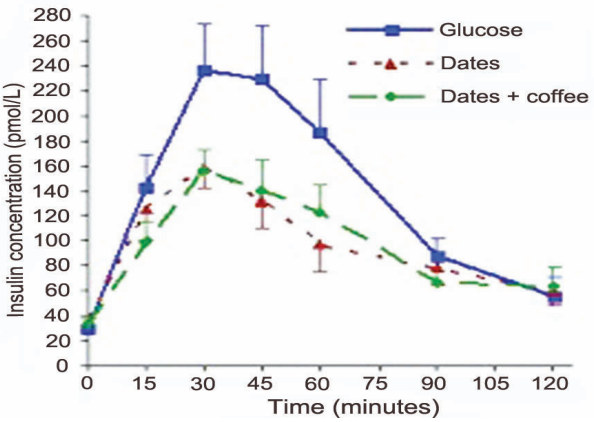

Figure 4 - Plasma insulin responses over 2 hours following consumption of reference glucose, dates, and dates with Arabic coffee. Results are presented as mean ± standard error of mean. Insulinemic index was measured using standard procedures.[19] A 2-factor (treatment and time) repeated measures ANOVA was used to analyze differences in the means of the insulin levels within the dates, dates with Arabic coffee, and standard glucose consumed. No significant differences were observed (p=1.00).

glucose levels occurred at 30 minutes for standard glucose, dates, and dates with Arabic coffee. At this time, the response to the standard glucose solution was significantly higher than the response to both dates, and dates with Arabic coffee (p=0.05, t=2.25). Similarly, the glucose response at 45 and 60 minute time points for subjects consuming dates with water was significantly lower (p=0.017, t=-2.93) than that for subjects consuming dates with Arabic coffee (p=0.041, t=-2.37). It appeared that Arabic coffee ingestion increased the glucose peak rise by approximately 0.4 mmol/L. The iAUC for plasma glucose concentrations over 2 hours postprandial period following consumption of standard glucose solution was 180 ± 13, for dates - 96 ± 11, and dates with Arabic coffee - 112 ± 11. From this, the GI for dates with water was found to be 55 ± 6, and dates with Arabic coffee was found to be 63 ± 5. The mean GI value for dates with water was lower than that for dates with Arabic coffee, however, the difference

did not quite reach statistical significance (p=0.08, t=-1.9, n=10). Plasma insulin for the standard glucose solution dates with water and dates with Arabic coffee peaked at 30 minutes after the ingestion of the foods, and then declined towards the baseline level by 120 minutes (**Figure** 4). Similar patterns were evident for all. The iAUC for plasma insulin concentrations was also calculated, and the II for dates with water was 64 ± 7, and for dates with Arabic coffee was 62 ± 8. The iAUC of insulin for dates with water and dates with Arabic coffee was much lower than that observed for standard glucose solution. This lower iAUC, however, was not sufficiently low enough to be significantly lower than the iAUC for glucose. There was no significant difference in the plasma insulin response between dates and dates with Arabic coffee (p=1.00, t=0.16).

Discussion. This study examined the impact of Saudi Arabian Khulas dates on glucose and insulin, with and without simultaneous consumption of Arabic coffee. The Khulas dates variety was chosen as it is the most famous variety consumed in Saudi Arabia.[20] Also, the GI of this variety has been reported previously, which can be used for comparison with our data.[13,15]

In this study, the GI value of 55 was obtained for Khulas dates and this compared well with previous studies.[13,15] It is well known that coffee contains many phenolic compounds such as CGA, which may have a potential effect on glucose and insulin levels.[3,6,7] The possible role of CGA in glucose metabolism could be due to the inhibition of glucose transporters (Na^+-dependent glucose transporter) or digestive enzymes (α-amylase and α-glucosidase), which could potentially influence the amount of glucose absorbed and reduce glucose release.[3] Also, consumption of coffee (400 mL containing 350 mg CGA) may affect the secretion of gastrointestinal peptides (glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) by decreasing GIP and increasing GLP-1, leading to slow intestinal glucose absorption.[7,21] In addition, the CGA may reduce plasma glucose output from the liver by inhibiting glucose-6-phosphatase activity.[3,6,21] The beneficial effects of CGA may appear at high concentrations of the coffee beverage, or for long periods of frequent coffee consumption. This might be the reason why we have not seen an effect in our study because it was a study examining the acute effects of coffee, or because the concentration of the Arabic coffee beverage was too low. This findings is similar to that of Louie et al.[22] They observed that there was no difference between the postprandial glucose and insulin levels of decaffeinated coffee versus water owing to a lower CGA content that was in the decaffeinated coffee beverage consumed. Nevertheless, it must be emphasized that the aim of this study was to study the effect of Arabic coffee as it is normally consumed rather than as a more concentrated beverage.

It is evident from other studies that the phenols, which are poorly absorbed from the human small intestine and are likely metabolized to their metabolites.[23] For example, approximately 33% of CGA is only absorbed and approximately two-thirds of it reach the colon, and may be metabolized to caffeic acid and quinic acid.[6] It has reported that the level of CGA that seems to have health benefits would range from 0.5-2.5 g/day.[1-5] Our LC-MS results for Arabic coffee have shown that the coffee used in this study certainly contained an array of CGA (**Figure 2**), but its total phenols' concentration was just 1.2 mmol/L. This concentration may have been too low to elicit a significant effect on plasma glucose and insulin levels. Our study has indicated that the consumption of coffee with dates exacerbates the plasma glucose response in healthy volunteers compared to the consumption of dates with water. In a similar way, an increase in the area under glucose and insulin curves and reduction in the insulin sensitivity has been observed with the ingestion of coffee with meals.[7-9] All these effects were proposed to be associated with the presence of caffeine in the coffee, which increases AUC of glucose and insulin.[8,9] Caffeine is a phosphodiesterase inhibitor which can increase the concentration of cyclic adenosine monophosphate (cAMP). Increased concentrations of cAMP have been associated with an impaired glucose tolerance after the consumption caffeinated coffee beverage.[7] Caffeine can also inhibit muscle glucose uptake as it acts as adenosine receptor antagonist.[6,24] It is clear that the consumption of Arabic coffee with dates had a modest effect bordering on a significant effect. In contrast to these short-term controlled trials, which have shown the effects of caffeine, this effect might be modified during long periods of coffee consumption among heavy and chronic coffee consumers.[3] Indeed, better glucose tolerance and a substantially lower risk of T2DM was associated with the high consumption of coffee.[2,3]

There are some limitations to this study. Clearly, this was an assessment of only one variety of dates and as such, it is quite a small study. However, the results provide useful information on a famous variety of dates consumed with Arabic coffee, which has not been reported previously. It is unfortunate that there are no insulinemic data on dates, or dates consumed with coffee in order to create comparison with our findings.

In conclusion, consumption of dates with Arabic coffee is a traditional practice in Saudi Arabia. We found that this habit of ingestion dates, at the same time with drinking Arabic coffee, increased slightly glucose response (p=0.08) in healthy people. This effect may due to the presence of caffeine, which has been found to impair glucose tolerance and decreases insulin sensitivity in previous clinical trials. As such, these findings could be applied on people with diabetes, and we would assume that consumption of dates would have an effect on plasma glucose levels in diabetic individuals similar to that effect seen in healthy people. The influence of the coffee beverage indicates that some detrimental effects can occur, and consumption of a decaffeinated coffee may be wise. Further research, particularly long term studies, may be required to ascertain the clear detrimental effect of dates with Arabic coffee on blood glucose, insulin, and triglycerides levels. In addition, as our coffee was caffeinated coffee, it is useful to investigate the effect of decaffeinated Arabic coffee on blood glucose and insulin levels.

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