Metabolic consequences of date snack before a meal: A traditional Arab practice

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ABSTRACT

Background: We have previously reported that contrary to the popular belief, ingestion of dates does not adversely affect glucose tolerance compared to an isocaloric Saudi breakfast in normal subjects.

Objective: Since Saudi people customarily consume dates prior to major meals, we considered it important to study the metabolic impact of the ingestion of combination of dates and a Saudi breakfast (a "combo meal"), and to compare its effect to those of date meal (DM) alone, Saudi breakfast (SBF) alone and oral glucose tolerance test (OGTT).

Methods: Nine subjects, 4 males and 5 females, aged 26.7 ± 0.8 years (mean ± SEM) with a body mass index of 22.4 ± 0.5 were fed in random order: (a) a DM consisting of approximately 300 calories (CHO 74.5g, protein 3.7g and fats 0.66g), (b) a SBF consisting of 300 calories (CHO 35.6g, protein 13.16g and fats 11.9g), (c) a 75g glucose solution (OGTT) and (d) a combination ("Combo meal") of DM and SBF as in (a) and (b) above on 4 different days at least one week apart. Plasma glucose (G), insulin (I) and C-peptide (C) values were determined at -30, 0, and then every 30 minutes for 180 minutes. Glycemic indices (GI) for DM, SBF and the "combo meal" also were determined.

Results: GI area profiles after the "combo meal" were significantly (P=0.02) lower than those of OGTT but did not differ when compared to DM or SBF. I and C profile areas were significantly greater (p<0.05) following the "combo meal" than those following either the DM or SBF but did not differ those of the OGTT. GI of the "combo meal" was 65 and fell in between that for the DM (59) and SBF (79).

Conclusion: Despite ingestion of twice as many calories as those contained either in DM or SBF, the "combo meal" does not appear to adversely influence the glucose tolerance in normal subjects; however this is accompanied by relative hyperinsulinemia, the consequences of which remain to be ascertained.

Keywords: Dates, Glycemic Index, Metabolic Consequences, Date Snack.


Until recently, there had been no information available concerning the metabolic effects of ingestion of dates, the fruit of the tree Phoenix dactyliferae, in human subjects despite the historical, socio-economical and nutritional significance of this fruit. We reported the first study of the metabolic responses to ingestion of dates in normal individuals.1 Contrary to the usual belief, we refuted, in that study, the notion that ingestion of dates adversely affects glucose tolerance compared to a Saudi meal in normal subjects. It also provided the first documentation of the glycemic index (GI) for dates. For the "Khalas" variety of dates studied we reported a GI of 57.7 which was significantly lower...
Table 1 - Values (Mean ± SEM) for areas under G, I & C curves in response to ingestion of 4 different meals

<table>
<thead>
<tr>
<th></th>
<th>OGTT</th>
<th>DM</th>
<th>SBF</th>
<th>COMBO</th>
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<tbody>
<tr>
<td>Glucose (min x mmol/L)</td>
<td>237 ± 45</td>
<td>126 ± 19</td>
<td>91 ± 17*</td>
<td>102 ± 18*</td>
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<tr>
<td>Insulin (min x pmol/L)</td>
<td>48578 ± 13209</td>
<td>21878 ± 3821**</td>
<td>21271 ± 3927**</td>
<td>59452 ± 1696***</td>
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<tr>
<td>C-Peptide (min x nmol/L)</td>
<td>187 ± 26</td>
<td>100 ± 17**</td>
<td>97 ± 10**</td>
<td>197 ± 36***</td>
</tr>
<tr>
<td>GI</td>
<td>57 ± 8.6</td>
<td>79</td>
<td>64.6</td>
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* p = < 0.05 (compared with OGTT) based on a parametric & nonparametric analysis.
**p = < 0.05 (compared with either the DM or SBF) based on parametric analysis.
OGTT-Oral Glucose tolerance Test
DM-Date Meal
SBF-Saudi Breakfast
COMBO-Saudi Breakfast and combination of dates

than that for the Saudi breakfast which was 79. In that report, we stressed the need to gather similar data on diabetic patients using different varieties of dates consumed in the Middle East. Subsequently, Fumiyiwa et al have confirmed our previous observations in healthy Saudi subjects and extended their observations in subjects with NIDDM. Aside from remarkable similarities noted between the two subjects in the normal subjects Fumiyiwa et al reported a lack of adverse effects of date ingestion compared to isocaloric oral dextrose administration among NIDDM subjects.

Notwithstanding these preliminary observations, there is a great need to explore further the metabolic impact of date ingestion to replicate actual daily consumption patterns both among normal and diabetic subjects. Since Saudi people customarily consume dates as a premeal snack, we considered it important to study the metabolic consequences of ingestion of a combination of dates and a Saudi breakfast (a "combo meal"), and to compare its effects to those of a date meal (DM) alone, Saudi breakfast (SBF) alone and oral glucose tolerance test (OGTT). The specific aims of the study included: (a) to examine plasma G, I and C responses following an acute challenge of a "combo meal" ingestion, (b) to compare circulating G, I and C responses following a "combo meal" to those following a DM, SBF and OGTT alone. It is believed that this information will help formulate principle of healthy diet in normal Saudi subjects and also provide a physiological basis to design principles of diet therapy in Saudi diabetic patients.

Materials and methods. Nine normal Saudi subjects, 4 males and 5 females, aged 26.7 ± 0.8 years (mean ± SEM) with a body mass index (BMI) of 22.4 ± 0.5 were fed in a random order: (a) DM consisting of approximately 300 calories of "Khalas" variety dates (CHO 74.5g, protein 3.7g, fats 0.66g), (b) a SBF consisting of 300 calories (CHO 35.6g, protein 13.16g and fats 11.9g), (c) a 75g glucose solution (OGTT) and (d) a combination ("combo meal") of DM and SBF as in a and b above, on four different days, at least one week apart, in a metabolic unit. On the basis of detailed interviews of normal Saudi volunteers (resident physicians and hospital employees), we defined their usual breakfast and designed the same for the study. This consisted of orange juice, boiled egg, Arabic bread, hot whole milk and Arabic coffee, which we have designated as a modified urban Saudi breakfast. Plasma G, I and C values were determined at -30 minutes, zero minutes and then every 30 minutes for 180 minutes in relation to the administration of each diet.

"Khalas" dates cultivated on our hospital premises were harvested as tree-ripe fresh soft fruit. The fruit was harvested six month previously, washed thoroughly and after a lapse of 4 days only the medium ripe dates were stored at -20 degrees centigrade. Following an overnight thawing it was determined that the storage process had resulted in a net weight loss of 15% from dehydration. The subjects were fed 110g dates the next morning. Dry matter (88.7%) in "Khalas" dates is composed predominantly (76%) of CHO. The content of reducing sugars in this variety of dates is reported to be 51-59%. Simple sugars (mono and disaccharides) contained in "Khalas" dates consist of glucose 32.4%, fructose 27% and sucrose 16.8% and the net glucose/fructose ratio is 1.2. The approximate composition of 110g "Khalas" dates according to the published data is as follows: dry weight 98g, total CHO 74.5g, glucose 31.8g, fructose 26.5g, sucrose 16.5g, polysaccharide hydrolysate 7g, proteins 3.7g, fats 0.66g and fiber 2.4g.

Incremental areas above baseline for 180 minutes for G, I and C, as well as the GI for the DM, SBF and
the "combo meal" were determined. The incremental area under the curve was taken to be the area above the fasting value calculated geometrically. Any area beneath the fasting value was ignored.

The GI has been defined as the area under the plasma glucose response curve for a test food divided by the area under the plasma glucose curve for an equivalent amount of CHO derived from a standard reference food taken by the same individual x 100. The amount of available CHO in the DM and the reference food (glucose solution) was almost identical (75g), but in the SBF it was 35.6. GI for SBF was calculated as described by previous investigators. The contribution of each food item to the CHO content of the SBF was calculated (19.7g of the total CHO was derived from orange juice, 5.4g from milk, 0.6g from egg and 9.9g from Arabic bread). The proportion of CHO contributed by each item was multiplied by its GI, obtained from published data to give the item's contribution to the meal GI. The GI values of the individual food items were summed to give the total meal GI (19.7/35.6 x 80 for orange juice, 5.4/35.6 x 49 for milk and 9.9/35.6 x 99 for bread = total GI of 79 for the SBF).

Assays. Plasma G was determined in duplicate on a Hitachi 737 Analyzer by a standard hexokinase method. Plasma I and C were measured in duplicate by standard radio-immunoassay methods; insulin by the coat-a-count procedure (Diagnostic Products Corporation, Los Angeles, CA); C-peptide using RIA-mat C-peptide II kit (BYK-Sangtec Diagnostica, Dietzenback, RFA). For all tests, standard quality assurance procedure were employed.

Statistical Analysis. By design, it is a paired study in which the study parameters for each subject were measured for all four meals. Comparisons among the meals were computed pair-wise within each subject and then compiled across subjects for evaluation of statistical significance. Parametric methods were employed for testing these compiled comparisons. Analyses were also carried out in subgroups defined by age, BMI, and the phases of the menstrual cycle for the purposes of checking for subgroup-specific significances. Regression methods were employed for these analyses.

Summary statistics are given as the mean +/- standard error of the mean throughout the text. Results are also illustrated through the presentation of average G, I and C profiles.

Results. Table 1 shows the values (mean ± SEM) for areas under G, I and C curves in response to ingestion of OGTT, DM, SBF and "combo meal." G area profiles after the "combo meal" were significantly (p<0.02) lower than those of OGTT but did not differ when compared to DM or SBF. I and C profiles areas were significantly greater (p<0.05)
following the "combo meal" than those following either the DM or SBF but did not differ from those of the OGTT. GI for the DM was 57.7 ± 8.6 and that for the SBF it was 79. GI of the "combo meal" was 64.6 and fell in between that for the DM and SBF.

There were no differences detected within subgroups defined by age, BMI and the phases of menstrual cycle.

**Glucose Responses** (Figure 1). Following the administration of each of the four different meals, there was a striking similarity in the timing at which the peak in plasma glucose occurred; it was at +30 minutes. The magnitude of these peaks differed for the different meals, being the greatest for the OGTT and the least for the SBF (p=0.01) with that for the DM and combo meals falling in between.

The peak plasma G value following the DM was significantly greater than that for SBF (p = 0.02). However, curiously enough, following the "combo meal" the peak plasma G response and the areas under the glucose curve (AUGC) were no significantly higher than when either DM or SBF were administered singly. This suggests that the SBF alone or in combination with dates in some way modulates what otherwise could have been a significantly greater peak G response following the "combo meal" with twice as many calories and greater CHO content than either the DM or the SBF.

Whereas the glucose values had returned to the baseline earliest (at +90 minutes) following the SBF and the "combo meal," they did not do so till +120 minutes for the DM and +150 minutes for the OGTT. Once returned to their respective baseline values, glucose responses continued to do so for the OGTT, the DM and the "combo meal." However, interestingly enough and for reasons not readily apparent, there was a rebound increase in glucose responses for the duration of the study following the SBF. This observation underscores the need to continue the sampling longer to determine a stable pattern. Despite such a rebound increase, the AUGC for the SBF was smaller relative to the "combo meal" because of a relatively smaller peak value for the former. It is also apparent that the greatest incremental AUGC for the OGTT is accounted for by the highest peak it inscribed, as well as the longest duration required for a return to the baseline. These observations emphasize the importance of taking into account both factors, i.e., the peak attained and the time it takes for the curve to return to the baseline, in interpreting the differences in the AUGC following different meals.

**Insulin & C-peptide Responses** (Figures 2 & 3). In general, the relative inscriptions of the curves for I and C responses following each of the respective four meals was similar with a little crossover in the patterns. For all four meals there was a marked resemblance in the timings of peak attainment (+60 minutes) and a return towards the baseline (+180 minutes) for the I and C responses. For any given meal the peak I and C responses lagged 30 minutes relative to the G peak. A rank order incremental responses in I and C values was evident. I and C incremental responses were greatest for the "combo meal," least for the SBF with the DM and OGTT falling in between. For the "combo meal," the I and C responses were the largest despite the G responses being lower than those for either the OGTT or the DM (Table 1). Both I and C values were greatest at all time points for the "combo meal" and were statistically higher (p=0.02) than those for the SBF at +30, +60, +90, and +120 minutes.

Figures 2 and 3 also illustrate the comparisons for the peak I and C responses, respectively at +60 minutes. The peak I and C responses following "combo meal" were statistically higher (p=0.04) than following the DM and SBF. The peak C but not the I responses following OGTT were also statistically higher (p=0.04) compared to DM and SBF. Since the circulating I and C response areas were significantly less (p<0.05) following the DM and SBF than OGTT and the "combo meal" (Table 1), it is obvious that the DM and the SBF are less potent insulin secretagogues compared to OGTT and the "combo meal".

Again as noted earlier for the G responses, the relative differences observed in the I and C responses are explained both by differences in their peak values and the duration over which they remained above the baseline values.

Whereas the I values had essentially returned to the baseline by +180 minutes, the C values failed to do so. Indeed by this time the I and C values following the "combo meal" continued to remain substantially and statistically (p=0.01, "Combo meal" versus DM, SBF or OGTT for I, p=0.001, "Combo meal" versus DM, p=0.004, "Combo meal" versus SBF and p=0.05, "Combo meal" versus OGTT for C values) higher than the other meals. It is clear that this "combo meal" is a potent secretagogue for insulin compared to either DM or SBF.

**Discussion.** Information on the metabolic responses to ingestion of individual macronutrients or mixed meals in normal individuals is limited. Attention has been focused on the effects of these individual nutrients on glucose and insulin concentrations in non-diabetic and diabetic subjects and not on the food forms in which they are usually ingested. It is also becoming increasingly clear that there are interactions between different ingested nutrients that result in metabolic responses that cannot be predicted from those of the individual nutrients. Such interaction make the prediction of the metabolic responses to a defined mixed meal potentially difficult.
In normal subjects, the insulin secretory rate and the plasma insulin responses are primarily determined by the absolute ambient glucose concentration to which the beta cells of the pancreas are exposed. Most insulin secretion over a 24-h period is secreted during times of the day when ingested food is not being assimilated, the so-called basal insulin secretion. Superimposed on this regulation is a transient and brisk rise of insulin secretion in response to a rapid increment in glucose concentration referred to as the first-phase insulin secretion, which is observed in an isolated pancreas preparation or following a rapid intravenous glucose infusion.\textsuperscript{16} However, in the studies reported here, following ingestion of glucose or a mixed meal, these two phases become indistinguishable, but the increase in insulin concentration correlated closely with the increase in glucose concentration temporally. We have previously reported, the return of the insulin concentration to an overnight fasting value, following a mixed meal, is considerably slower than the return of the glucose concentration, i.e., there is a dissociation between the two.\textsuperscript{9} This has never been explained and may be related to non-glucose insulin secretogogues such as amino acids, possibly fructose but not glucose, and the incretin hormones secreted by gut mucosal cells in response to ingested nutrients.\textsuperscript{16,17} A dissociation between the insulin and glucose responses is again apparent in the present study in that the return of the insulin and C-peptide concentrations back to the fasting value was considerably slower than the return of the glucose concentration following each of the four meals. Such persistent elevations of insulin and C-peptides values were especially striking for the “combo meal” indicating that this meal is a potent insulin secretogogue compared to the other meals in the study. This fact is also reflected in the integrated insulin and C-peptide areas being significantly greater for the “combo meal” compared to the DM and the SBF.

A critical component of fuel homeostasis in the mammals is the tight regulation of insulin secretion from the beta-cells of the islets of Langerhans. Although glucose is widely recognize as the primary signal for insulin release in the postprandial phase, changes in the levels of other metabolic fuels (such as those present in a mixed meal), incretin hormones, and neuro-transmitters provide important amplification of the glucose signal.\textsuperscript{17} The importance of these is still not completely understood, nevertheless it is clear that they play an important role in glucose homeostasis and in the regulation of ingested fuel disposition. Commonly they potentiate the glucose stimulatory effect and by interacting with glucose they determine the insulin secretory response to meals. Additionally, dietary fats, as contained in mixed meals, may play a role in altering insulin and/or glucose response to an oral glucose load.\textsuperscript{16,17} These observations unrescore the need to study the glucose and insulin responses following mixed meals.

Our data confirm the previous observations that the qualitative increase in insulin concentration greatly exceeds the increase in glucose concentration.\textsuperscript{16} The maximal glucose concentration in our present studies typically did not exceed 65% of the pre-meal value, whereas the increase in insulin concentration was 300%. Overall, the system is designed to maintain the maximal circulating glucose concentration in the non-fed state within narrowly defined limits. Our data also indicate that the system is also designed to allow only a modest rise in glucose after a variety of meals and to rapidly restore the glucose concentration to the non-fed state; this is impressively true for the “combo meal” despite containing greater calories and more carbohydrates. There are many reasons for the system to be designed so. A chronically elevated glucose or large, relatively sustained elevations in glucose concentration after a meal may be physiologically undesirable. One of the most important of these would be the deleterious consequences of the chemical reactivity of the aldehydic group on the glucose molecule.\textsuperscript{16}

We became interested in determining glucose and insulin responses to various macronutrients in normal individuals for four reasons. First, because amino acids stimulate insulin secretion directly without increasing the glucose concentration significantly,\textsuperscript{13,16} dietary sources of these may prove useful in the management of NIDDM patients. Secondly, because fats, proteins, and possibly non-glucose carbohydrates stimulate a rise in incretin hormones,\textsuperscript{16,17} we were interested in determining whether the addition of these foods to a glucose meal could facilitate insulin secretion to a glucose meal and thus reduce the circulating glucose response to glucose-yielding foods; a concept supported by the data presented in this study. It should be noted that the pattern of incretins released are different to different foods,\textsuperscript{16} therefore, this concept appealed to be a likely possibility.\textsuperscript{9} Thirdly, we have previously demonstrated that in normal subjects, the plasma glucose concentration is elevated above an overnight fasting value for only 1-3 h after a mixed meal.\textsuperscript{9} However, in people with NIDDM, this time is extended to > 4h, and the excursions above the fasting glucose concentration are much larger.\textsuperscript{16} Thus, any mechanism for reducing the postprandial glucose rise is likely to be important in preventing or delaying the long-term complications of diabetes that have been associated with a high glucose concentration. Lastly, if hyperinsulinemia is playing a role in the long-term cardiovascular population studies,\textsuperscript{18} it is important to understand the plasma
insulin response to various meals. In this regard, the demonstration of greater insulin area following "combo meal", are of interest; however the implications of such "hyperinsulinemia" are clearly beyond the scope of the study.

With additional investigations it will be possible to explain quantitatively the glucose and insulin responses to various defined mixed meals unique to different cultural and ethnic groups. Such studies should provide insight into the mechanisms by which fuel storage and utilization are regulated in the postprandial state. They also should provide insight into the regulation of other hormones important in fuel metabolism such as glucagon, cortisol, growth hormone, and possibly catecholamines and incretins in healthy and diabetic subjects. For example we have clearly shown an increase in serum cortisol in non-diabetic people after ingestion of mixed meals high in protein. Our previous work and those of others also provide supportive evidence to suggest that an incretin response to ingested protein is of major importance in insulin secretion, although the data are indirect.

Studies of the metabolic responses to individual absorbed macronutrients and defined foods and the effect of their incorporation into mixed meals should provide a basis for the development and evaluation of diets for people with diabetes in long-term studies. It is hoped that investigations such as this will ultimately lead to dietary recommendations for diabetic patients that are based on firm scientific data.

References


