Comparison of a protein-rich diet with a low-glycaemic index diet on glucose control. Implications for diabetic and non-diabetic subjects.

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Abbreviations

AUC	Area under the curve
BG	Blood glucose
CGMS	Continuous glucose monitoring system
GI	Glycaemic index
GL	Glycaemic load
IGT	Impaired glucose tolerance
MAGE	Mean amplitude glycaemic excursion
PR	Protein-rich

Running title: Protein rich diet vs. low-GI diet

Abstract

The effects of three different diets on glucose variability were investigated in healthy male subjects. Glucose concentration was recorded using the continuous glucose monitoring system in eight volunteers, following a randomized crossover repeat-measure design. Three diets were designed using commonly eaten foods to be a low-glycaemic index (GI) diet or a high-GI diet or a protein-rich (PR) diet. Diets were consumed for 24h and glucose concentrations were concomitantly recorded. Over the measurement period, the glycaemic responses to the PR and low-GI diets were similar. At lunch and dinner time, the PR diet produced modest elevations of glucose concentration post-prandially compared to the other two diets. Nocturnally, the glycaemic profile under the PR diet increased when the glycaemic profiles for the other diets remained relatively constant. The results of the study indicate that a protein-rich diet was capable of modulating blood glucose comparable to that seen when fed a low-GI diet. At a time when there is continued and popular interest in a low-GI diet, an alternative diet that serves to provide comparable glycaemic control is a useful addition to our dietary portfolio.

Introduction

The diabetes epidemic has been linked with a concomitant epidemic in obesity. The expression "diabesity" has now been proposed [1]. Epidemiological studies have shown that both type 2 diabetes and obesity increase morbidity [2] and mortality [3]. Several randomized trials have indicated that changes in dietary practice, lifestyle and behaviour can have a significant impact on health outcomes [4-6]. Diabetes and obesity, collectively, represent the two most important chronic diseases globally [7].

Poor glycaemic control has been recognized to increase the risks of micro- and macro-vascular damage and therefore the risk of coronary heart disease [8]. The results of the DECODE study suggested that the postprandial glycaemic response was a better predictor of cardiovascular diseases than the fasting glucose value alone [9]. More recently, it has been proposed that continuous daily glycaemic excursions predisposed individuals to impaired glucose tolerance and subsequently to diabetes and CVD [10-12]. These observations suggest that a diet-based strategy to minimize glycaemic excursions is a useful and practical alternative to pharmacological interventions. Moreover, identifying diets that provide modest glycaemic excursions may also play an important role in the management and treatment of pre-diabetic and diabetic subjects [13].

In recent years, low-glycaemic index foods and diets have been recommended as dietary advice to normal, pre-diabetic and diabetic subjects in order to optimize glycaemic control. The glycaemic index (GI), first introduced in 1981 [14], is a classification of the blood glucose-raising potential of the carbohydrates in foods. It is defined as the incremental area under the blood glucose curve of a 50g carbohydrate portion of a test food expressed as a percentage of a standard (reference) food taken by the same subject [15]. A low-GI diet has been successfully used in the management and treatment of obesity and diabetic subjects [10-12]. Despite its recent popularity and wide use, it has been suggested that a low-GI diet is both monotonous and difficult to comply [16]. Any strategy to improve dietary compliance and afford dietary variability, without compromising glycaemic control would be major advantage.

With this in mind, the current study investigated the possibility of using a protein-based diet to increase variety and ascertain whether such a diet also had the ability and scope to maintain good glycaemic control.

Material and methods

Subjects

Eight, healthy Caucasian male subjects were recruited for the study. The exclusion criteria were medical conditions or the use of medications known to affect glucose regulation or appetite. Ethical approval for the study was obtained from the University Research Ethics Committee of Oxford Brookes University. All subjects were explained the purpose of the study and gave written informed consent prior to participation.

Study design

In a randomized cross-over repeat-measure design, subjects were prescribed for 24h a low-GI diet, a high-GI diet or a protein-rich (PR) diet on three separate occasions, separated by at least a week. The diets included commercially available, common foods and were closely matched as possible for their total energy content. The nutritional analysis of the diets is provided in Table 1. The type and amount of protein foods used in the PR diet was based on the quantities customarily consumed by UK subjects. Subjects ate and drank only the food and drinks provided, except for water, which was consumed *ad libitum*. Table 2 provides a detailed breakdown of the quantities and type of the foods in the low and high-GI diets along with the protein-rich diet. The food components in each category were identical apart from the foods categorized as low/high-GI or protein-rich. The classification of low and high-GI foods was based on the international GI tables [17] and our work [18,19]. Meals were prepared in the diet

kitchen at the Nutrition and Food Science Group, Oxford Brookes University. Breakfast and lunch were eaten in the laboratory; subjects were allowed to eat snacks and dinner at home that were provided by the researchers.

Glucose measurement

The continuous glucose monitor system (CGMS™, Medtronic MiniMed, Northridge, CA, USA) has been designed to measure and record glucose values from the interstitial fluid. Interstitial glucose concentration is detected through an electrochemical reaction using a glucose oxidase probe anchored on a disposable sensor. The CGMS™ sensors were inserted according to the manufacturer's instructions [20]. The CGMS™ sensor was fitted at 08:00 h on the experimental day and was removed the following day at 11:00 h by trained personal.

On each day of the study, subjects were instructed to take six finger-prick capillary blood glucose measurements to calibrate the CGMS™ using the Unistik®2 single-use lancing device (Owen Mumford, Oxford, UK). Blood glucose was measured using the HemoCue® system (HemoCue AD, Sweden). In order to stabilize the sensor and obtain reliable values, only values from 11.00 h onward were included. The data reported here represent 245 glucose readings for each individual between 11:00 h to 06:00 h the next day.

Evaluation of the glycaemic response and variability

The overall glycaemic response can be characterised by either the mean glucose concentration or the area under the curve (AUC) [21]. Although the use of AUC is not necessary in the case of equally spaced measurements (i.e. CGMS™) [21], AUC have been previously used in the literature to describe similar data (total AUC [22] and incremental AUC [23]). The effects of the diets on the glucose response were examined for the entire measuring period (~20 hours) and for three distinct periods of the day (lunch, dinner and night time). The AUC were calculated using the trapezoid method as recommended by the FAO/WHO [15]. Both absolute and incremental glucose values were used. Values at 22:00 hours (night time) were used as baseline figures. Using these values, incremental AUC (iAUC) were then calculated.

Several indicators have been developed and used to ascertain glycaemic control (variability) [24] and the risk of developing hypo- or hyperglycaemia [25]. In this study, two of these indicators were applied to the data as they represented various aspects of glycaemic variability:

(1) The standard deviation (SD) is an estimate of the variability within the sample. The SD represented the glycaemic variability over the measuring period without considering the effect of time.

(2) The mean amplitude glycaemic excursion (MAGE) is in fact the average value of the main glycaemic excursions. Only excursions, which deviate more than ± 1SD of the mean glycaemia, were included. This index is calculated using cumulative values taken every 15min.

Mathematical descriptions of these indicators can be found in Table 3.

Power calculation

Brynes et al. recommended a minimum of eight data sets to detect a 15% change in the area under the 24 h glucose curve using a power of 85% and a probability level of 5% [26]. In our study, a total of eight subjects were also therefore used.

Statistical analysis

Statistical analysis was performed using Prism version 4.00 for Windows (GraphPad Software, Inc, San Diego, CA, USA). All data were tested for normality using the Kolmogorov-Smirnov test and expressed as mean ± SEM, unless stated otherwise. One-way repeated-measure ANOVA were performed and the assumption of sphericity was tested using the Mauchly's test of sphericity. If this assumption was violated, the Greenhouse-Geisser correction was applied instead. Bonferroni's multiple comparison post-hoc test was applied. Statistical significance was set at $P \leq 0.05$.

Results

Subjects characteristics

The characteristics of the subjects are presented in Table 4. All subjects were known to be healthy. Their average age was 39.2 ± 5.7years, BMI 25.0 ± 0.8kg.m^{-2}. The mean fasting blood glucose was 4.98 ± 0.13mmol.l^{-1}.

Glycaemic profiles

The glycaemic profiles for the three diets are graphically presented in Figure 1. Whilst the timings of eating episodes were similar under each dietary condition within each subject, they were clearly not the same between subjects. Figure 1 shows the postprandial glycaemic responses for lunch, dinner and the overnight (from 22.00 hours until 06.00 hours) glycaemic response. For clarity and ease of observation, the inter-meal glycaemic profiles have not been presented in the graph. However, the complete data set was used for the other analyses presented here.

166

167 Overall effects of the three diets

168 Firstly, the fasting glucose concentrations were not significantly different prior to the feeding
169 of the three diets (P=0.4288; low-GI: 4.8 ± 0.2; high-GI: 5.0 ± 0.2 and PR: 5.0 ± 0.2mmol.l^{-1}).
170 Table 5 shows the average glucose concentrations and the corresponding AUC for the entire
171 period of study (~20hours).
172 The absolute mean glucose value was the lowest for the PR diet. The incremental value and
173 iAUC of the PR diet were comparable to that of the low-GI diet. Not unexpectedly, with
174 reference to iAUC, the high-GI diet produced a 25-fold difference (PR: -0.01/low-GI: -0.02
175 vs. high-GI: 0.52mmol.l-1). None of these results however reached statistical significance
176 (P>0.05).
177

178 Glycaemic response for the different periods of the day

179 The same parameters were used to describe the glycaemic responses for lunch, dinner and
180 nocturnally (22:00 hours – 06:00 hours). The results are presented in Table 6.
181 For lunch, the pre-meal baselines were lower for the high-GI and PR diets than for the low-GI
182 diet. The 2-hour postprandial mean value on the PR diet was smaller than on the low-GI or
183 high-GI diets. These results were also not significant (P>0.05). However, the incremental
184 mean glucose value and iAUC were significantly different between the diets (P=0.0238 and
185 P=0.0239, respectively). The values for the low-GI and PR diets were very similar but the
186 post-hoc test showed that that difference detected was only significant between the low-GI
187 and high-GI diets (P<0.05).
188 For dinner, the pre-meal baselines were similar between the three diets. With regards to the
189 metabolic parameters discussed above, the PR diet consistently exhibited smaller results
190 compared to the other two diets. Whilst none of these parameters reached significance
191 (P>0.05), the iAUC was marginally significant (P<0.1).
192 Finally nocturnally (22:00 hours – 06:00 hours), the glucose value was the lowest on the PR
193 diet. The incremental mean glucose value and iAUC were greater for the PR diet than for the
194 other two diets. Most of these results failed to reach significance (P>0.05), except for iAUC
195 (marginally, P<0.1).
196

197 Glucose variability: standard deviation (SD) and mean amplitude glycaemic excursions
198 (MAGE)

Table 7 shows the results for the parameters of glycaemic variability. The SD of the high-GI diet was the largest. Interestingly, the MAGE values for both high-GI and PR diets were negative, indicating a general tendency to lower glucose concentrations. However, on closer examination, the larger SEM for the high-GI MAGE suggest that the glycaemic excursions occurred more frequently and were more intense on "both sides" of the MAGE cut-off values (± 1SD). The SD and the results for MAGE presented no significant difference (P>0.05).

Discussion/conclusions

The objective of the study was to compare the effects of three different diets (low-GI, high-GI and protein-rich diets) on glycaemic response over a prolonged period (~20hours). These results indicate that the conventionally held view that it is only a low-GI diet that can be used to minimize glycaemic excursions has been challenged. It is evident that a protein-based diet that is both acceptable and palatable can also elicit similar low glycaemic response. The proposed protein-rich foods used in the study were commonly available and widely eaten. An examination of the percentage of energy derived from protein of such diet (Table 1) also indicates that it is not necessary to consume a large amount of protein to gain its lower glycaemic response advantage. As a time point, the influence of the lunch intake on the glycaemic response was very significant as the low-GI and PR diets produced comparable and modest iAUCs in contrast to the high-GI diet. Similarly at dinner, the PR and low-GI diets produced smaller iAUCs compared to the high-GI diet. Finally, the nocturnal iAUCs showed an interesting pattern with the subjects on the PR showing a gradual increase in glycaemia. Indeed, this observation has been previously reported [27,28].

A resurgence of interest in a low-carbohydrate, high-protein diet has emerged with the popularity of the Atkins diet. It is well recognized that the rise in circulating glucose concentration after the consumption of a mixed meal is due to the glucose that is absorbed after the breakdown and digestion of starch-containing foods. Low-GI foods (e.g., legumes, dried fruits, whole grains, seeds) are known to elicit a lower postprandial blood glucose response due to the slower breakdown and release of carbohydrates [29].

The relationship between branched-chain amino acid and glucose metabolism was first investigated in relation to its association with the glucose-alanine cycle [30]. Layman and co-workers demonstrated that a protein-rich diet not only improved glucose control but also reduced the postprandial insulin response [31]. The regulation of blood glucose within a narrow

of 4.5 to 6mmol.l^{-1} demands a precise balance between hepatic release of glucose and tissue glucose utilization.

The results of our study indicate that the use of a protein-rich diet was capable of modulating blood glucose comparable to that seen when fed a low-GI diet. Given the relatively small (N=8) sample size of our study, our results must be viewed as a preliminary report. Nonetheless, it is an important observation that illustrates that the use of a protein-rich, palatable diet may be useful recommendation to those desiring to control blood glucose. Moreover, as far as the authors are aware, this is the first study to compare the efficacy of a protein-rich diet with a low-GI diet over a prolonged period (~20 hours) to examine their long-term glycaemic response. At a time when there is continued and popular interest in a low-GI diet, an alternative diet that serves to provide comparable glycaemic control is a useful addition to our dietary portfolio. Whilst its long-term use and application in free-living subjects remains an area for future research, these results indicate that a protein-rich diet may be a useful alternative to a low-GI diet in diabetics and pre-diabetics aiming to control their glucose profiles.

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Tables and figure

Table 1. Nutritional analysis of the three experimental diets

Diet	Energy kJ	Protein g (%E)	Carbohydrate g (%E)	Fat g (%E)	Dietary fibre g	Sodium mg	GI	GL
Low-GI	7272	77.8 (18.2)	206.8 (45.5)	68.3 (34.8)	27.3	1358	35	70
High-GI	7182	58.1 (13.8)	233.2 (52.0)	64.3 (33.1)	10.0	1938	97	163
PR	6005	121.7 (34.5)	139.4 (37.1)	45.0 (27.7)	13.0	868	36	64

259 Table 2. Food provided in the three diets

Low-GI diet	Quantity (g)	High-GI diet	Quantity (g)	Protein-rich diet	Quantity (g)
Lunch:		Lunch:		Lunch:	
Soy-linseed bread	80	Plain bagel	85	Beef sirloin, roasted	175
Cheddar	45	Cheddar	45	Cheddar	45
Cucumber	24	Cucumber	24	Cucumber	24
Lettuce	10	Lettuce	10	Lettuce	10
Low fat spread	30	Low fat spread	20	Apple	100
Apple	100	Apple	100	Unsweetened apple juice	200
Unsweetened apple juice	200	Sweetened apple juice	200	Dinner:	
Dinner:		Dinner:		Egg tagliatelle	50
Egg tagliatelle	100	Jacket potatoes	150	Bolognese sauce (with extra meat)	200
Bolognese sauce	200	Bolognese sauce	200	Apple	100
Apple	100	Jam doughnut	65	Snacks:	
Snacks:		Snacks:		Sultanas	80
Cashew nuts	50	Digestive biscuits	60		
Dried apricot	50	Pop corn	20		
Fruit yogurt	120				
Grapes	50				

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262 Table 3. Definition of the formulae used to describe glucose variability

Name	Formulae	Description
AUC	$AUC = \frac{1}{2} \times \sum_{i=0}^{n-1} (t_{i+1} - t_i)(x_i + x_{i+1})$	x_i: values of the variables at t_i, n: the number of measurement. AUC: area under the curve
MAGE	$MAGE = \frac{1}{n} \sum (BG_i - BG_{i-1})$ if $\Delta BG_i \notin (-SD, +SD)$	BG_i: glucose concentration at t_i

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265 Table 4. Subjects' characteristics (mean ± SEM)

Age (years)	Height (m)	Weight (kg)	BMI ($kg.m^{-2}$)	Body fat (%)	Fasting BG ($mmol.l^{-1}$)
39.2 (± 5.7)	1.79 (± 0.04)	79.7 (± 3.0)	25.0 (± 0.8)	19.2 (± 1.7)	4.98 (± 0.13)

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268 Table 5. Effect of the diets on glycaemic response over the measuring period (mean ± SEM)

	Absolute mean ($mmol.l^{-1}$)	Incremental mean ($mmol.l^{-1}$)	iAUC ($mmol.l^{-1}.min^{-1}$)
Low-GI	4.65 (± 0.22)	-0.02 (± 0.22)	253 (± 95.5)
High-GI	4.58 (± 0.22)	0.52 (± 0.22)	849 (± 310)
PR	4.38 (± 0.23)	-0.01 (± 0.23)	335 (± 134)
P-values	0.1460	0.2040	0.1143

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Table 6. Characteristics of the glycaemic responses of the lunches, dinners and at night time (mean ± SEM)

	Pre-meal baseline ($mmol.l^{-1}$)	2h post-prandial mean ($mmol.l^{-1}$)	2h post-prandial Incremental mean ($mmol.l^{-1}$)	iAUC ($mmol.l^{-1}.min^{-1}$)
Lunch				
Low-GI	4.76 (± 0.26)	4.85 (± 0.27)	0.08 (± 0.06) *	21.4 (± 5.14) *
High-GI	4.10 (± 0.27)	4.67 (± 0.27)	0.56 (± 0.18) *	76.5 (± 21.2) *
PR	4.19 (± 0.25)	4.30 (± 0.21)	0.88 (± 0.14)	28.3 (± 12.2)
P-values	0.1816	0.1548	0.0238	0.0229
Dinner				
Low-GI	4.20 (± 0.21)	4.73 (± 0.22)	0.52 (± 0.11)	66.3 (± 13.6)
High-GI	4.34 (± 0.18)	4.91 (± 0.22)	0.58 (± 0.18)	74.1 (± 21.4)
PR	4.31 (± 0.26)	4.41 (± 0.26)	0.11 (± 0.14)	30.8 (± 8.61)
P-values	0.8191	0.1530	0.0909	0.1015
Night time				
Low-GI	4.79 (± 0.21)	4.76 (± 0.20)	-0.03 (± 0.10)	52.6 (± 24.6)
High-GI	4.68 (± 0.29)	4.69 (± 0.29)	0.01 (± 0.11)	74.2 (± 29.4)
PR	4.26 (± 0.10)	4.56 (± 0.15)	0.30 (± 0.14)	157 (± 49.8)
P-values	0.1100	0.7316	0.1145	0.0808

(*: difference between the conditions as shown by the post-hoc test)

276 Table 7. Average SD and MAGE values for the three diets (mean ± SEM)

	SD ($mmol.l^{-1}$)	MAGE ($mmol.l^{-1}$)
Low-GI	0.45 (± 0.09)	0.11 (± 0.09)
High-GI	0.60 (± 0.09)	-0.05 (± 0.19)
PR	0.50 (± 0.05)	-0.09 (± 0.10)
P-values	0.4142	0.3870

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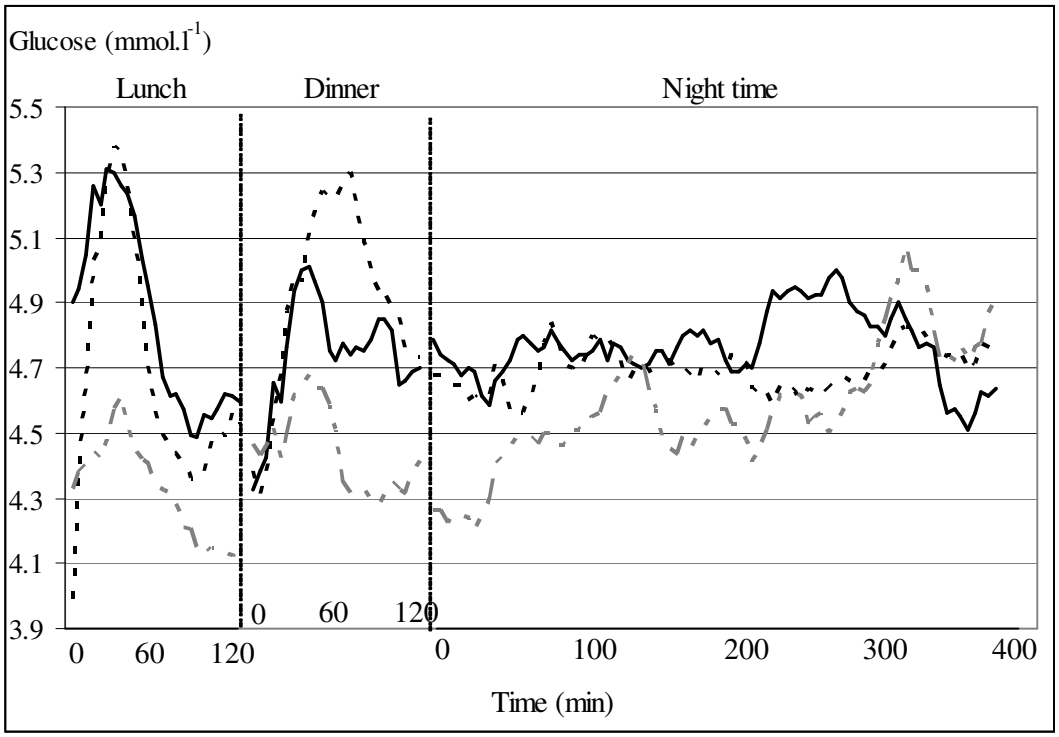
Figure 1. Postprandial glycaemic responses for lunch and dinner and nocturnal glycaemic profile



The X-axis is divided in three sections. For lunch and dinner, it represents the 2-hour postprandial glycaemic response (0 to 120min) and for night time, the glycaemia between 22:00 hours and 06:00 hours on the following day (0 to 400min). The continuous black line (——) represents the glycaemic profile of the low-GI diet; the dashed black line (– –), the high-GI diet and the grey dashed line (– –), the PR diet.

302 References

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304 1. Astrup, A. & Finer, N. (2000) Redefining type 2 diabetes: 'diabesity' or 'obesity
305 dependent diabetes mellitus'? *Obes Rev* **1**, 57-59.

306 2. Hu, F. B. et al. (2001) Diet, lifestyle, and the risk of type 2 diabetes mellitus in
307 women. *New Engl J Med* **345**, 790-797.

308 3. St-Onge, M.-P. & Heymsfield, S. B. (2003) Overweight and obesity status are linked
309 to lower life expectancy. *Nutr Rev* **61**, 313-316.

310 4. Pan, X. R. et al. (1997) Effects of diet and exercise in preventing NIDDM in people
311 with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. *Diabetes Care* **20**,
312 537-544.

313 5. Tuomilehto, J. et al. (2001) Prevention of type 2 diabetes mellitus by changes in
314 lifestyle among subjects with impaired glucose tolerance. *New Engl J Med* **344**, 1343-1350.

315 6. Knowler, W. C. et al. (2002) Reduction in the incidence of type 2 diabetes with
316 lifestyle intervention or metformin. *New Engl J Med* **346**, 393-403.

317 7. Mendez, M. A., Monteiro, C. A. & Popkin, B. M. (2005) Overweight exceeds
318 underweight among women in most developing countries. *Am J Clin Nutr* **81**, 714-721.

319 8. Mohsin, F. et al. (2005) Discordant trends in microvascular complications in
320 adolescents with type 1 diabetes from 1990 to 2002. *Diabetes Care* **28**, 1974-1980.

321 9. DECODE Study Group (1999) Glucose tolerance and mortality: comparison of WHO
322 and American Diabetic Association diagnostic criteria. *Lancet* **354**, 617-621.

323 10. Salmeron, J. et al. (1997) Dietary fiber, glycemic load, and risk of NIDDM in men.
324 *Diabetes Care* **20**, 545-550.

325 11. Salmeron, J. et al. (1997) Dietary fiber, glycemic load, and risk of non-insulin-
326 dependent diabetes mellitus in women. *JAMA* **277**, 472-477.

327 12. Ludwig, D. S. et al. (1999) High glycemic index foods, overeating, and obesity.
328 *Pediatrics* **103,** E26.

329 13. Leiter, L. A. et al. (2005) Postprandial glucose regulation: new data and new
330 implications. *Clin Ther* **27**, S42-56.

331 14. Jenkins, D. J. et al. (1981) Glycemic index of foods: a physiological basis for
332 carbohydrate exchange. *Am J Clin Nutr* **34**, 362-366.

333 15. FAO/WHO expert consultation (2001) Carbohydrates in human nutrition.

16. Sloth, B. et al. (2004) No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet. *Am J Clin Nutr* **80**, 337-347.

17. Denyer, G., Dickinson, S. & Brand-Miller, J. (2006) Home of the glycemic index [internet] available from http://www.glycemicindex.com/ . 18 October 2007.

18. Henry, C. J., Lightowler, H. J., Strik, C. M., Renton, H. & Hails, S. (2005) Glycaemic index and glycaemic load values of commercially available products in the UK. *Brit J Nutr* **94**, 922-930.

19. Henry, C. J., Lightowler, H. J., Strik, C. M. & Storey, M. (2005) Glycaemic index values for commercially available potatoes in Great Britain. *Brit J Nutr* **94**, 917-921.

20. Mastrototaro, J. (1999) The MiniMed Continuous Monitoring System (CGMS). *J Pediatr Endocrinol Metab* **12**, 751-758.

21. Matthews, J. N., Altman, D. G., Campbell, M. J. & Royston, P. (1990) Analysis of serial measurements in medical research. *Brit Med J* **300**, 230-235.

22. Brynes, A. E., Adamson, J., Dornhorst, A. & Frost, G. S. (2005) The beneficial effect of a diet with low glycaemic index on 24h glucose profiles in healthy young people as assessed by continuous glucose monitoring. *Brit J Nutr* **93**, 179-182.

23. Henry, C. J., Lightowler, H. J., Tydeman, E. A. & Skeath, R. (2006) Use of low-glycaemic index bread to reduce 24-h blood glucose: implications for dietary advice to non-diabetic and diabetic subjects. *Int J Food Sci Nutr* **57**, 273-278.

24. Guerci, B. (2003) [Asymptomatic glycemic instability: how to measure it and which clinical applications?] article in French. *Diabetes Metab* **29**, 179-188.

25. Kovatchev, B. P., Clarke, W. L., Breton, M., Brayman, K. & McCall, A. (2005) Quantifying Temporal Glucose Variability in Diabetes via Continuous Glucose Monitoring: Mathematical Methods and Clinical Application. *Diabetes Technol Ther* **7**, 849-862.

26. Brynes, A. E. et al. (2003) A low glycemic diet significantly improves the 24h blood glucose profile in people with type 2 diabetes, as assessed using the continuous glucose MiniMed monitor. *Diabetes Care* **26**, 548-549.

27. Winiger, G., Keller, U., Laager, R., Girard, J. & Berger, W. (1995) Protein content of the evening meal and nocturnal plasma glucose regulation in type-I diabetic subjects. *Horm Res* **44**, 101-104.

28. Gannon, M. C., Nuttall, F. Q., Saeed, A., Jordan, K. & Hoover, H. (2003) An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. *Am J Clin Nutr* **78**, 734-741.

29. Björck, I., Granfeldt, Y., Liljeberg, H., Tovar, J. & Asp, N. (1994) Food properties affecting the digestion and absorption of carbohydrates. *Am J Clin Nutr* **59**, 699S-705S.

30. Ruderman, N. B. (1975) Muscle amino acid metabolism and gluconeogenesis. *Annu Rev Med* **26**, 245-258.

31. Layman, D. K., Shiue, H., Sather, C., Erickson, D. J. & Baum, J. (2003) Increased dietary protein modifies glucose and insulin homeostasis in adult women during weight loss. *J Nutr* **133**, 405-410.