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NUTRIENT INTERACTION IN RELATION TO GLYCAEMIC AND INSULINAEMIC RESPONSE

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Abstract : Although it is known that protein, fat and fibre reduce the postprandial glycaemia following an oral carbohydrate load, the nature and extent of interaction of different nutrients with one another in this respect is not well understood. The present study was designed to explore systematically the glycaemic and insulinaemic response to glucose (G) alone, or in combination with one or more of the following : casein (CS), maize oil (MO), cellulose (CL) and pectin (P). Besides 100 g G, eleven isoenergetic and six isocarbohydrate meals were studied on healthy adult males using an incomplete block design. Addition of other nutrients to G led to a lowering of the glycaemic response. The lowest glycaemic responses were seen in case of meals containing the largest number of nutrients. P was more effective in reducing postprandial glycaemia than CL. As in case of glycaemic response, low insulinaemic responses were also associated with P-containing meals, and meals containing the largest number of nutrients. But unlike in case of glycaemic response, there was a tendency for elevation of the insulinaemic response in case of CL-containing meals.

The degree of attenuation of glycaemic response observed with meals containing several nutrients was roughly predictable on the basis of the attenuation observed with meals in which only one nutrient had been added at a time to G. But the glycaemic response of natural foods is unlikely to be predictable on the basis of their nutrient composition because of the overriding influence of several other factors such as physical form, cooking, processing, storage and antinutrient content of the food.

Key words : cellulose dietary fibre glucose tolerance test glycaemic index pectin

INTRODUCTION

The overall blood glucose level may be considered an integrated average of the fasting and postprandial glucose levels. Therefore, designing meals with a low glycaemic response is now an established method for achieving good glycaemic control in diabetics (1). The glycaemic response to a food may be quantified in terms of the area under the blood glucose curve (AUC-G) following ingestion of the food as a percentage of the AUC-G following a reference food, such as glucose (2) or white bread (3, 4). The figure resulting from this calculation has been termed the glycaemic index (GI). Based on the GI of a large number of foods, it has been proposed that the GI of a food is inversely related to the protein, fat and fibre content of the food (2, 5). Thus it appears that all major non-carbohydrate nutrients interact with carbohydrates in a food in an important way to determine its GI. If the effect of each nutrient, and the nature of its interaction with other nutrients, can be determined and quantified, it may be possible to predict the GI of foods from their nutrient composition. The present study is a systematic exploration of glycaemic response to meals containing glucose (G) alone, or in combination with one or more of the following : casein (CS), maize oil (MO), cellulose (CL) and pectin (P). Parts of this extensive study have been published earlier (6, 7, 8, 9).

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METHODS

Subjects

The studies were conducted on a pool of 25 normal, healthy human male volunteers (age 18-42 years, weight 44.0-72.5 kg, height 162.0-180.5 cm).

Experimental design

Besides 100 g G, eleven isoenergetic and six isocarbohydrate meals were studied for their glycaemic and insulinaemic response (Table I). Since the total number of meals was too large to be studied on any individual, the meals were grouped into six isoenergetic and two isocarbohydrate sets using an incomplete block design. Each set had either five or six meals. Glucose was one of the meals in every set, and each of the other meals generally occurred in at least two sets. Five volunteers were enlisted for each 5-meal set, and six volunteers for each 6-meal set. Some volunteers participated in more than one set. The 5 or 6 meals comprising a set were administered in a preplanned random sequence using a 5 × 5 or 6 × 6 Latin Square design respectively.

TABLE I : Composition of meals studied.

S. No.	Glucose (g)	Casein (g)	Maize oil (g)	Cellulose (g)	Pectin (g)	Energy (KJ)
1.	100	—	—	—	—	1680
		A. Isoenergetic meals (400 kcal)				
2.	60	40	—	—	—	1680
3.	60	20	9	—	—	1680
4.	100	—	—	20	—	1680
5.	100	—	—	—	20	1680
6.	60	40	—	20	—	1680
7.	60	40	—	—	20	1680
8.	60	20	9	20	—	1680
9.	60	20	9	—	20	1680
10.	60	—	18	—	—	1680
11.	60	—	18	20	—	1680
12.	60	—	18	—	20	1680
		B. Isocarbohydrate meals (100 g glucose)				
13.	100	20	—	—	—	2016
14.	100	20	9	—	—	2352
15.	100	20	—	20	—	2016
16.	100	20	—	—	20	2016
17.	100	20	9	20	—	2352
18.	100	20	9	—	20	2352

Meals

Meals were formulated using different combinations of one or more of the following components: G (Glucose-D; Glindia Ltd, Bombay) CS (SISCO Research Laboratories, Bombay), MO (Cornola; Ballarpur Industries, Chandrapur), nutrition grade CL (CSIR Biochemicals Unit, New Delhi), and P (SISCO Research Laboratories, Bombay). The amount of each constituent was as indicated in Table I. The meals were constituted in 200 ml water 0.5 h before ingestion. Additional 200 ml water was provided for drinking with the meal.

Meal tolerance tests

On the morning of the test, the volunteer reported after an overnight fast. After taking a fasting venous blood sample, the meal was provided, and was consumed within 10 min at a steady rate. The midpoint between starting and finishing the meal was taken as zero time. Blood samples were drawn at 0.5, 1.0, 1.5 and 2.0 h.

Analysis

All blood samples were analysed for glucose concentration by the o-toluidine method, and for insulin concentration by double antibody radioimmunoassay.

Serial estimations of serum glucose and insulin were further used for deriving the incremental area under the 2-h glucose curve (Δ AUC-G) and the incremental area under the 2-h insulin curve (Δ AUC-I).

Δ AUC-G and Δ AUC-I were calculated by using a programmable calculator (Hewlett Packard 41 CV). The glycaemic index (GI) was calculated using the formula :

$$\text{Glycaemic index} = \frac{\Delta \text{ AUC-G in response to the meal}}{\Delta \text{ AUC-G in response to 100 g glucose}} \times 100$$

Similarly the insulinaemic index was calculated using the formula :

$$\text{Insulinaemic index} = \frac{\Delta \text{ AUC-I in response to the meal}}{\Delta \text{ AUC-I in response to 100 g glucose}} \times 100$$

Ethical considerations

The protocol of the study was approved by the Ethics Committee of the All India Institute of Medical Sciences. An informed written consent was obtained prior to enlisting a subject for the study.

RESULTS

The glycaemic indices of the meals studied have been shown in Figs. 1 and 2. In spite of the marked

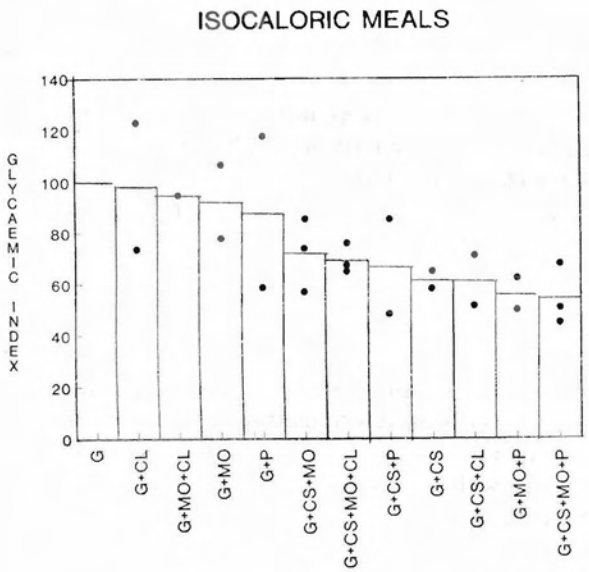

Fig. 1 : Glycaemic indices of the isoenergetic meals studied arranged in descending order of the overall mean glycaemic index (GI). Each point represents the mean GI observed in one set comprising 5 or 6 subjects. Since each meal generally occurred in 2 or 3 sets, there are 2 or 3 points for each meal. The height of each bar corresponds to the overall mean GI for each meal.

inter-set variation, there was a clear trend for a lowering of the glycaemic response by the addition of other nutrients to G. The lowest glycaemic responses were seen in case of meals containing the largest number of nutrients. The pectin-containing meal G+CS+MO+P had a lower glycaemic index than the cellulose-containing meal G+CS+MO+CL. Further, both these four-component meals had the least inter-set variation.

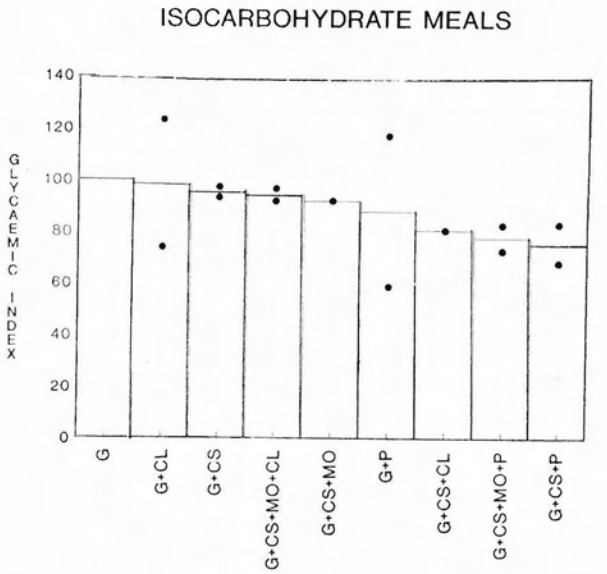

Fig. 2 : Glycaemic indices of isocarbohydrate meals studied arranged in descending order of the overall mean glycaemic index. The data for G+CL and G+P is the same as in Fig. 1 because these meals are both isoenergetic and isocarbohydrate. Other details as in Fig. 1.

The insulinaemic indices of the meals studied have been shown in Figs. 3 and 4. As in case of

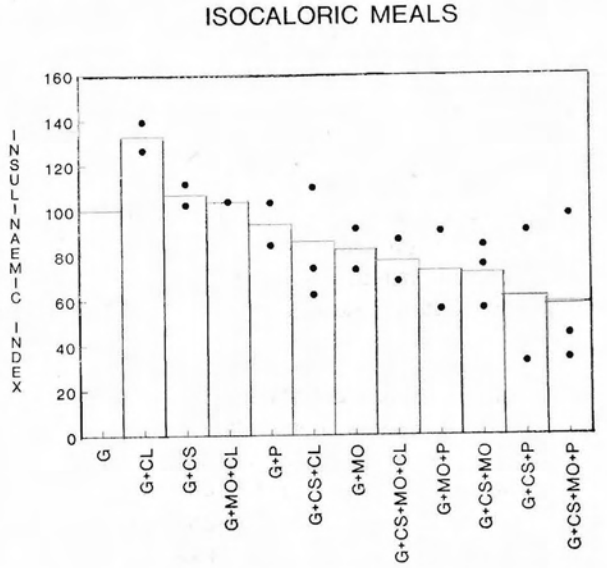

Fig. 3 : Insulinaemic indices of isoenergetic meals studied arranged in descending order of the overall mean insulinaemic index. Other details as in Fig. 1.

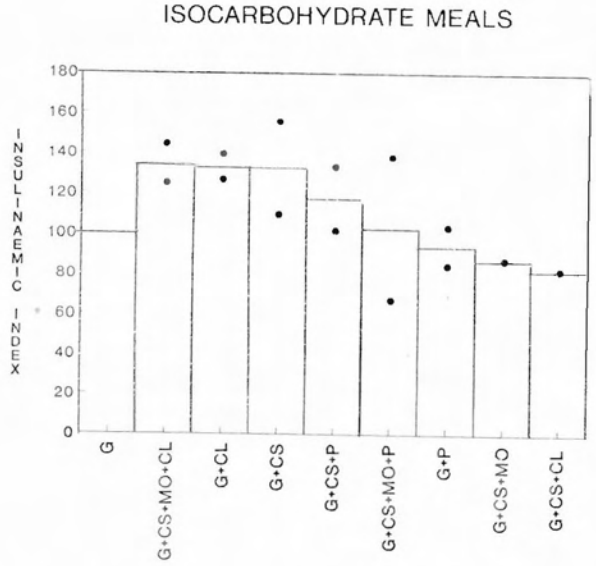

Fig. 4 : Insulinaemic indices of isocarbohydrate meals studied arranged in descending order of the overall mean insulinaemic index. The data for G+CL and G+P is the same as in Fig. 3 because these meals are both isoenergetic and isocarbohydrate. Other details as in Fig. 1.

glycaemic index, low insulinaemic indices were also associated with pectin-containing meals and meals containing the largest number of nutrients. But unlike in case of glycaemic index, there was a clear tendency for elevation of insulinaemic index in case of meals containing CL.

DISCUSSION

The present study is a systematic investigation of the effect of protein, fat and fibre on postprandial glycaemia and insulinaemia. Further, it looks at the interaction of these nutrients with one another in this respect.

The nurtients were studied in isoenergetic and isocarbohydrate combinations. The isoenergetic combinations were studied from a practical standpoint. The energy intake of an individual is kept constant at the level of requirements but food composition may be varied. Hence isoenergetic combinations were studied to find the best way in which the energy intake may be distributed to achieve the lowest postprandial glycaemia and insulinaemia. The isocarbohydrate meals were studied from a more strictly scientific point of view. The aim was to see how the glycaemic and insulinaemic response to 100 g G is modified by further addition of protein, fat and fibre, singly or in different combinations.

There was general agreement between the results obtained with isoenergetic and isocarbohydrate combinations. The magnitude of the glycaemic response to a given mixed meal was generally lower in case of isoenergetic combinations than in case of isocarbohydrate combinations. This was possibly due to the quantity of G being 40 g less in most of the isoenergetic meals (Table I). However, in general, the addition of any nutrient to G resulted in a reduction in postprandial glycaemia. Coingestion of more than one additional nutrient was more effective in this respect than that of any nutrient singly. This suggests that each added nutrient reduces postprandial glycaemia at least partly through independent mechanisms.

Proteins may reduce postprandial glycaemia by at least two mechanisms. Firstly, proteins and amino acids have been reported to stimulate insulin secretion (10,11,12,13). Secondly, some amino acids compete with glucose for intestinal transport (14). The latter mechanism would slow down intestinal glucose absorption, and thereby reduce the necessity for insulin secretion as well. Thus the effect of proteins on insulin secretion would depend upon the net result of the two opposing mechanisms mentioned above, and possibly some additional mechanisms. Probably that explains conflicting reports in literature suggesting that proteins stimulate (10, 11, 12) or have no significant effect (15) on insulin secretion.

Fats are also likely to reduce postprandial glycaemia by at least two mechanisms. Firstly, fats slow gastric emptying, and thereby reduce the rate of delivery of carbohydrate to the small intestine. This would slow down glucose absorption and consequently reduce postprandial glycaemia as well as insulinaemia. Secondly, fats stimulate GIP secretion (16), which in turn stimulates insulin secretion. Fats also stimulate cholecystokinin (CCK) secretion, which may potentiate the insulinotropic effect of GIP (17). Thus, as in case of proteins, fats are also likely to be less consistent in their effect on postprandial insulinaemia than on glycaemia.

The effect of *cellulose* on postprandial glycaemia is neither marked nor is its mechanism well understood. Cellulose, is a non-viscous, water-insoluble fibre, and such fibres do not affect postprandial glycaemia significantly (6,7,18). However, the present study suggests that cellulose might stimulate insulin secretion. It is possible that cellulose stimulates GIP secretion, which in turn stimulates insulin secretion. This hypothesis is based on the fact that CL is a glucose polymer, and the terminals of its molecules may provide appropriate ligands for the same receptors which mediate the GIP releasing effect of glucose.

Pectin is a water soluble, viscous fibre, and has been reported to reduce postprandial glycaemia (6,18,19). Pectin slows down gastric emptying (18), and this is thought to be the major mechanism by which it reduces postprandial glycaemia. In addition, it might also pose a mechanical barrier to absorption by increasing the thickness of the unstirred water layer (20).

The mechanisms by which various nutrients affect postprandial glycaemia or insulinaemia have been summarised in Table II. Since the mechanisms are partly distinct, it is possible that the effects of nutrient combination may be mathematically predictable. In order to test this hypothesis, the data on simple two-nutrient combinations from all isocaloric sets has been pooled to evaluate the mean reduction in AUC-G brought about by each nutrient (Table III).

TABLE II : Effect of nutrients on postprandial glycaemia and insulinaemia.

Nutrient	*Mechanism*	*Effect on*	
		Postprandial glycaemia	*Postprandial insulinaemia*
Protein	Stimulation of insulin secretion	Reduction	Increase
	Competitive inhibition of glucose absorption	Reduction	Reduction
Fat	Slowing of gastric emptying	Reduction	Reduction
	GIP secretion*	Reduction	Increase
Cellulose	? GIP secretion	Reduction	Increase
Pectin	Slowing of gastric emptying	Reduction	Reduction
	Mechanical barrier		

*The effect of GIP may be potentiated by cholecystokinin (CCK) which is also secreted in response to dietary fat during the postprandial phase (Zawalich 1988).

TABLE III : Contribution of individual nutrients to reduction in postprandial glycaemia.

*Meals compared**	*Nutrient evaluated*	*Number of sets***	*Mean % reduction in Δ AUC-G*
G vs G+CS	CS	3	33.2
G vs G+MO	MO	2	21.3
G vs G+CL	CL	2	4.4
G vs G+P	P	2	21.9

*Isoenergetic meals
**Each set had 5 or 6 subjects

Next, the reduction observed in response to three- or four-nutrient combinations has been compared to the reduction predicted for those combinations mathematically (Table IV). The predicted reduction has been calculated taking into account the amount of each nutrient in the combination. For example, 40 g casein in G+CS brought about a 33.2% reduction in Δ AUC-G, and 18 g maize oil brought about a 21.3% reduction in Δ AUC-G. Therefore, in response to G+CS+MO, which incorporates 20 g CS and 9 g MO, the predicted reduction in Δ AUC-G is (0.5 x 33.2) + (0.5 x 21.3) = 27.2%. As seen in Table IV, the observed reduction is somewhat greater than the predicted reduction. Estrich et al (10) also showed that protein and fat together gave a greater reduction in postprandial glycaemia than the sum of the individual effects of protein and fat.

TABLE IV : Predictability of response to multiple nutrients.

*Meals compared**	*Number of sets***	*Mean % reduction in Δ AUC-G*	
		Observed	*Predicted**
G vs G+CS+MO	3	32.0	27.2
G vs G+CS+MO+CL	3	34.5	31.6
G vs G+CS+MO+P	3	64.5	49.1

*Predicted change is the algebraic sum of weighted changes in response to individual nutrients as indicated in Table III.
**Each set had 5 or 6 subjects.

Thus in the present study, the glycaemic response to a meal can be predicted fairly accurately from its nutrient composition. But these results apply only under the conditions of the study, which are much simpler than in case of natural foods. The issue was explored from a different angle in another study : if

glycaemic response depends on nutrient composition, different foods having identical nutrient composition should (but may not) have the same glycaemic response (21). In this study, it was found that the glycaemic response to bread, potato, rice and green gram was higher than that to respective fabricated meals having identical carbohydrate (as corn flour), protein (as casein), fat (as maize oil) and fibre (as ispaghula husk) content. Hence in real foods, nutrient composition is a poor predictor of glycaemic response. This is quite understandable because, besides its nutrient content, the glycaemic response to a food is significantly affected by the type of starch it contains (22, 23), its salt content (24, 25), its antinutrient content (26, 27, 28), its non-nutrient chemical content (29, 30), its physical state (31, 32), the way it has been cooked or processed (33, 34, 35), the duration of chewing (36), starch-protein interactions (37), and antecedent diet (38).

The insulinaemic response was not predictable even under the simplified conditions of the present study. This may be because the same nutrient might affect insulin secretion in opposite directions through different mechanisms (Table II). That may also explain the high degree of variability observed in the insulinaemic response, as well as the observation that glycaemic and insulinaemic responses to meals are not necessarily parallel (39, 40).

Although the variability of response was less in case of glycaemic response, it was still considerable (Table V). The intra-individual variation was no less than the inter-set and inter-individual variations. Thus the population of subjects may be considered homogenous with respect to the tests performed, and the variability is likely to be inherent in the test. This conclusion is supported by high variability of the same order reported in glucose tolerance test by West et al (41) and Harding et al (42). One of the factors responsible for the variability may be nature of the meal eaten on the evening before the glucose or meal tolerance test. Carbohydrate tolerance has been reported to be better when low GI foods were eaten on the evening before the test than if high GI foods were eaten (43). However, we found that neither the results of glucose tolerance test nor of the bread meal tolerance test were significantly affected by the addition of 50 g butter to the meal eaten on the evening before the test (44). Yet another factor responsible for intra-individual variation may be the consistent observation that the glycaemic response during a tolerance test is higher when the subject reports for such a test for the first time (45, Bijlani et al, unpublished). On the second turn, the test loses its novelty, making the subject less apprehensive, and therefore possibly reducing the subject's adrenalin secretion. Hence the glycaemic response has a 'false' high level when the subject undergoes a tolerance test for the first time, irrespective of the meal administered.

TABLE V : Variability in glycaemic response to 100 g glucose.

Type of variability	*Coefficient of variation (%)*		
	0.5 h	*2.0 h*	*AUC-G*
Inter-individual*	18.8	22.8	17.2
Inter-set	8.5	14.2	11.1
Intra-individual	16.2	19.8	16.8

*For only one set having 6 subjects

To summarize, maximum reduction in postprandial glycaemia may be achieved by adding the largest variety of other nutrients to dietary carbohydrate. Such a diet would be not only suitable for diabetics but also desirable for the 'normal' population because there is no clear dividing line between the two population groups. Normal individuals may be able to prevent diabetes by adopting a low glycaemic index diet. However, predicting the glycaemic index from nutrient composition of foods may not be possible because of our poor understanding of all the factors which determine glycaemic response. At present there is no short cut to determining the GI of individual foods, and it would be still better to determine the GI of different dishes made from each food.

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