Modulation of postprandial glycaemia and insulinaemia by cellulose in mixed nutrient combinations

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The present study was designed to examine the effect of cellulose (CL) on postprandial glycaemia and insulinaemia when ingested with glucose (G), casein (CS) and maize oil (CO) in various combinations. The study was conducted on five healthy male volunteers, on each of whom five meal tolerance tests were performed. The meals were isoenergetic and consisted of G; G and CL; G, CS and CL; G, CO and CL; G, CS, CO and CL. The meals were administered after an overnight fast. In addition to a fasting venous blood sample, blood was collected 0·5, 1·0, 1·5 and 2·0 h after ingestion for measurement of serum glucose and insulin levels. The glycaemic response to G + CS + CL and G + CS + CO + CL was significantly lower, while the insulinaemic response to G + CL was significantly higher than that to G. Addition of CL to G did not alter the glycaemic response, but accentuated the insulinaemic response. Further addition of CS in isoenergetic meals attenuated the glycaemic response, which may be because of a reduction in the amount of G in the meals. Like CS, CL also seemed to have an insulinotropic effect. The mechanism of the insulinotropic effect of CL cannot be deduced from the present study, but it is possible that like G, CL also stimulates gastric inhibitory peptide (GIP) secretion from the duodenum, which in turn stimulates insulin secretion.

Cellulose: Glucose tolerance test: Glycaemic index.

Studies in the recent past have crystallized the concept that reduced postprandial glycaemia and insulinaemia are valid and rational goals to aim at while designing diets for the prevention and treatment of diabetes (Jenkins *et al.* 1982; Collier *et al.* 1986; Thorburn *et al.* 1986). One of the methods for achieving these goals is the supplementation of high-carbohydrate meals with dietary fibre (Jeffrys, 1974; Jenkins *et al.* 1977; Potter *et al.* 1981; Sartor *et al.* 1981; Florholmen *et al.* 1982; Blackburn *et al.* 1984; Jarjis *et al.* 1984; Sahi *et al.* 1985; Sud *et al.* 1988). The fibres reported to be the most useful in reducing postprandial glycaemia are viscous, water-soluble varieties such as guar gum (Jenkins *et al.* 1977, 1978; Blackburn *et al.* 1984; Jarjis *et al.* 1984) and pectin (Jenkins *et al.* 1977, 1978; Vaaler *et al.* 1980; Sahi *et al.* 1985), but not water-insoluble non-viscous varieties such as cellulose (Jenkins *et al.* 1978; Sahi *et al.* 1985). While acute studies have generally shown that cereal fibre does not affect postprandial glycaemia, some long-term studies suggest that cereal fibre may improve glucose tolerance (Villaume *et al.* 1984; Bijlani *et al.* 1985). Further, in vitro studies using everted intestinal sacs have shown that cellulose, a major constituent of cereal fibre, impairs glucose uptake by the gut (Bijlani *et al.* 1986; Mahapatra *et al.* 1988). In view of the discrepancies between acute glycaemic response studies on the one hand, and the long-term and in vitro studies on the other, the present work was designed to study the effect of cellulose on postprandial glycaemia and insulinaemia when ingested with glucose, casein and maize oil in various combinations.

* For reprints.

METHODS

The study was conducted on five healthy male volunteers (age 19–21 years, weight 50–69 kg, height 1·66–1·77 m). They were studied after an overnight fast on five mornings at weekly intervals. After a fasting venous blood sample had been drawn, they were administered one of the five isoenergetic 'meals', shown in Table 1, in different sequences in accordance with a Latin-square design. The meals were formulated using glucose (G; Glucose-D: Glindia Ltd, Bombay), maize oil (CO; Cornola; Ballarpur Industries, Chandrapur), casein (CS; SISCO Research Laboratories, Bombay) and cellulose (CL; CSIR Biochemicals Unit, New Delhi). The meals were prepared on the morning of the test, by hydration, 0·5 h before ingestion. The meals were provided in a standardized 400 ml volume.

Each meal was consumed within 5 min at a steady rate. The mid-point between starting and finishing the meal was taken as zero time. Venous blood samples were drawn at 0·5, 1·0, 1·5 and 2·0 h. Serum was separated within 0·5 h and analysed for glucose concentration on the same day by the o-toluidine method. The remaining serum was stored at $-20°$ for measurement of insulin concentration by radioimmunoassay.

Calculations

Serial estimations of serum glucose and insulin were further used to derive the following indices: area under the 2 h glucose curve (AUC-G) and area under the 2 h insulin curve (AUC-I), corresponding incremental areas ($\triangle$AUC-G and $\triangle$AUC-I), glycaemic index (GI) (Jenkins et al. 1981) and insulinaemic index.

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

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

Similarly the insulinaemic index was calculated using the formula:

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

Statistical analysis

The observed and computed variables following different meals were compared by analysis of variance (ANOVA). The points at which a significant difference between meals could be expected on the basis of ANOVA analysis were subjected to Newman–Keuls' multiple-range test (Armitage, 1971). Newman–Keuls' test is a rather conservative multiple-range test and, therefore, sometimes misses even some fairly marked differences. To minimize the chances of missing genuine differences, paired comparisons by Student's t test were also made between each meal and the control (glucose meal). This was considered reasonable even in a multiple-test situation, because using the response to 100 g glucose as the reference for comparison was built into the protocol of the study. ('When comparisons are made which flow naturally from the plan of the experiment or survey the usual t test is appropriate' (Armitage, 1971).)

Ethical considerations

The experimental protocol of the study had the previous approval of the Ethics Committee of the All India Institute of Medical Sciences. The participation was on a strictly voluntary basis, and the subjects knew that they could withdraw from the study at any stage. Every volunteer gave his informed written consent before being admitted to the study.

Table 1. *Composition of the experimental meals*

Meal	G (g)	CS (g)	CO (g)	CL (g)	Energy (KJ)
G	100	—	—	—	1680
G+CL	100	—	—	20	1680
G+CS+CL	60	40	—	20	1680
G+CO+CL	60	—	18	20	1680
G+CS+CO+CL	60	20	9	20	1680

G, glucose; CS, casein; CL, cellulose; CO, maize oil.

Table 2. *Glycaemic response to the isoenergetic meals tested using healthy adult male subjects*

(Mean values with their standard errors for five subjects)

	Serum glucose (mg/l)										AUC-G (g/l. min)		△AUC-G (g/l. min)	
	0 min		30 min		60 min		90 min		120 min					
Meal†	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
G	784	18	1288	79	1242	48	1076	106	1010	89	137	3·9	43	3·4
G+CL	740	30	1338	67	1268	71	1098	106	1068	74	141	6·2	52	8·7
G+CS+CL	754	34	1170	112	1054	116	924	64	810*	61	121	9·0	30	10·0
G+CO+CL	762	13	1302	96	1148	19	976	43	896	46	131	4·7	39	5·0
G+CS+CO+CL	804	38	1058	31	1186	55	1042	49	908	60	125*	3·6	28	5·0

G, glucose; CL, cellulose; CS, casein; CO, maize oil; AUC-G, area under the 2 h glucose curve; △AUC-G, incremental area under the 2 h glucose curve.

* $P < 0.05$ (by paired t test).

† For details, see Table 1.

RESULTS

The glycaemic and insulinaemic responses obtained in response to various meals are given in Tables 2 and 3, and Figs 1 and 2. The values of various computed indices are given in Table 4. Multiple comparisons revealed very few significant differences between meals. The significant differences referred to below were revealed, except where indicated, by paired comparison of some meal-responses with the response to G.

When 20 g CL were added to the G load (G+CL) the glycaemic response became more pronounced, although not significantly. Insulin levels in response to G+CL were higher than those in response to G at 0·5 h ($P < 0.05$) and 2·0 h ($P < 0.02$) and its AUC-I was also higher ($P < 0.05$).

Isoenergetic substitution with 40 g CS (G+CS+CL) gave a significantly blunted glycaemic response compared with G at 1·0 h ($P < 0.10$) and 2·0 h ($P < 0.05$).

If the isoenergetic substitution was made with 18 g maize oil and cellulose (G+CO+CL), the glycaemic as well as insulinaemic response was not significantly different from that to G.

The four-component meal, namely G+CS+CO+CL, gave the lowest glycaemic level at 0·5 h, which was significantly lower ($P < 0.05$) than that in response to G (paired t test)

Table 3. *Insulin response to the isoenergetic meals tested using healthy adult male subjects*

(Mean values with their standard errors for five subjects)

| Meal† | Serum insulin (μU/ml) | | | | | | | | | | AUC-I (mU/ml. min) | | $\triangle$AUC-I (mU/ml. min) | |
| | 0 min | | 30 min | | 60 min | | 90 min | | 120 min | | | | | |
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
G	42	17	368	68	724	215	562	119	466	145	5·7	0·9	5·2	0·8
G+CL	60	21	714*	120	812	148	662	148	556*	136	7·7*	1·3	7·0	1·3
G+CS+CL	14	09	498	121	618	158	570	164	382	65	5·9	1·3	5·7	1·2
G+CO+CL	44	23	578	174	516	202	574	172	328	105	6·0	1·9	5·5	1·8
G+CS+CO+CL	22	10	416	125	680	90	590	185	408	147	5·8	1·1	5·6	1·0

G, glucose; CL, cellulose; CS, casein; CO, maize oil; AUC-I, area under the 2 h insulin curve; $\triangle$AUC-I, incremental area under the 2 h insulin curve.

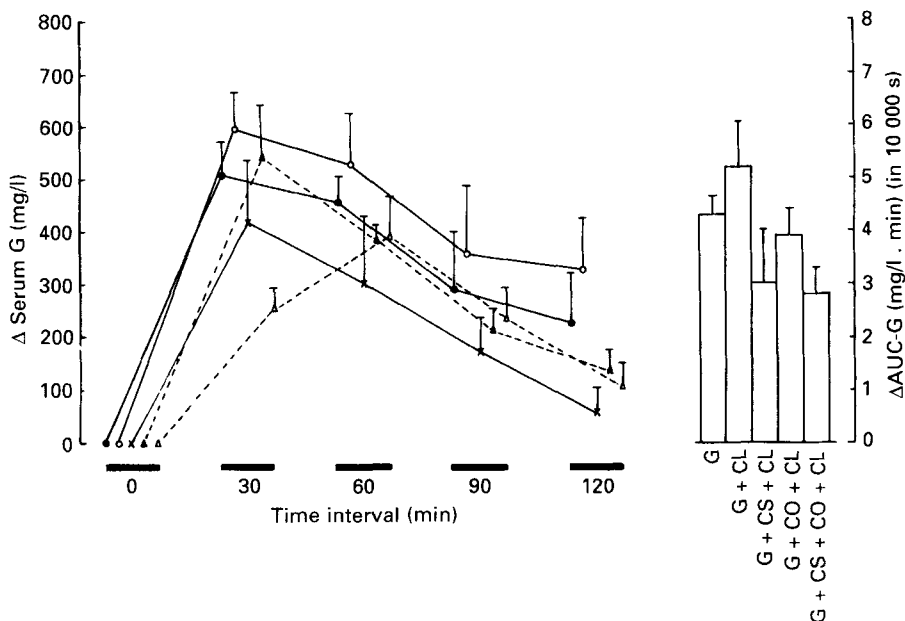* $P < 0.05$ (by paired t test).
† For details, see Table 1.

Fig. 1. Serum glucose (G) response to the meals administered to five healthy adult male subjects. G ($\bullet$——$\bullet$), G+cellulose (CL) ($\bigcirc$——$\bigcirc$), G+casein (CS)+CL ($\times$——$\times$), G+maize oil (CO)+CL ($\blacktriangle$----$\blacktriangle$) and G+CS+CO+CL ($\triangle$----$\triangle$). Points are mean values, with their standard errors represented by vertical bars. For details of meals and procedures, see Table 1 and p. 132. $\triangle$AUC-G, incremental area under 2 h G curve.

and G+CL (ANOVA). The AUC-G was also significantly lower in response to G+CS+CO+CL than in response to G. G+CS+CO+CL was the only meal which gave the glycaemic peak at 1·0 h.

Thus, addition of CL to G does not alter the glycaemic response but leads to significantly higher insulin levels.
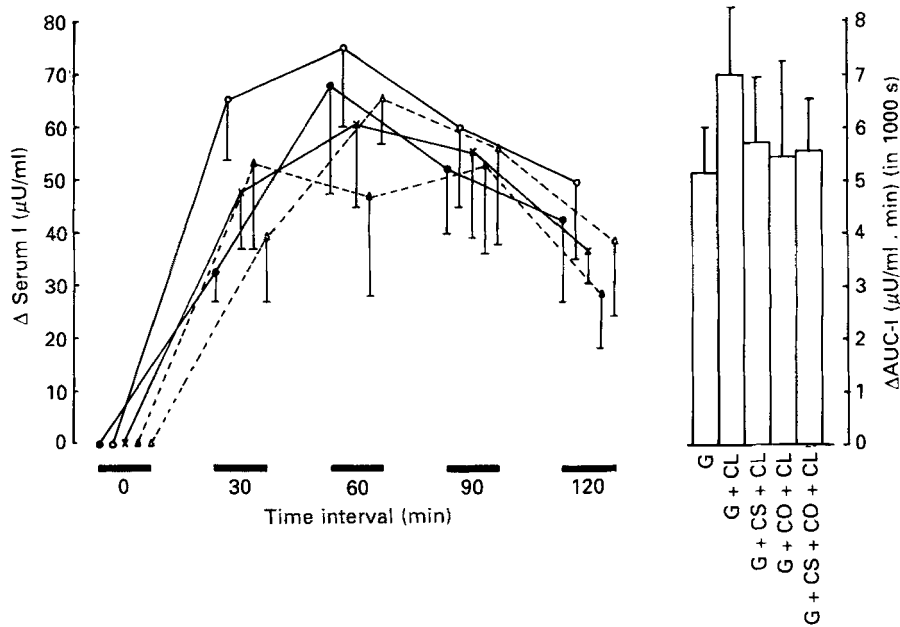
Fig. 2. Serum insulin (I) response to the meals administered to five healthy adult male subjects. Glucose (G) (●——●), G + cellulose (CL) (○———○), G + casein (CS) + CL (×——×), G + maize oil (CO) + CL (▲----▲) and G + CS + CO + CL (△----△). Points are mean values, with their standard errors represented by vertical bars. For details of meals and procedures, see Table 1 and p. 132. △AUC-I, incremental area under 2 h I curve.

Table 4. *Indices of glycaemic and insulin response to the isoenergetic meals tested using healthy adult male subjects*

(Mean values with their standard errors)

Meal*	GI†		△GI		Insulinaemic index‡		△ Insulinaemic index	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
G	100	0·0	100	0·0	100	0·0	100	0·0
G + CL	103	5·0	123	21·3	141	14·6	140	15·3
G + CS + CL	88	6·8	71	22·3	104	13·5	110	11·3
G + CO + CL	96	5·3	95	14·8	101	19·0	103	23·9
G + CS + CO + CL	91	2·6	67	13·4	106	19·1	113	23·0

G, glucose; CL, cellulose; CS, casein; CO, maize oil; GI, glycaemic index; △GI, glycaemic index based on incremental areas.

* For details, see Table 1.

† $\dfrac{\text{Area under 2 h glucose curve in response to meal}}{\text{Area under 2 h glucose curve in response to 100 g G}} \times 100.$

‡ $\dfrac{\text{Area under 2 h insulin curve in response to meal}}{\text{Area under 2 h insulin curve in response to 100 g G}} \times 100.$

DISCUSSION

Addition of CL to G did not alter the glycaemic response appreciably. This is consistent with previous studies where postprandial glycaemia was not reduced by co-ingestion of water-insoluble non-viscous fibres such as cellulose (Jenkins *et al.* 1978; Sahi *et al.* 1985), when compared with water-soluble viscous fibres such as pectin (Jenkins *et al.* 1976, 1977, 1978; Sahi *et al.* 1985) and guar gum (Jenkins *et al.* 1976, 1977, 1978; Blackburn *et al.* 1984; Jarjis *et al.* 1984). The impairment of G uptake by everted intestinal sacs in the presence of CL (Bijlani *et al.* 1986) represents the study of only a small segment of intestine. In the intact organism, the great length of the small intestine provides an extensive reserve which can overcome a marginal impairment of absorption. The improvement in G tolerance observed in some long-term studies with high-fibre cereals (Villaume *et al.* 1984; Bijlani *et al.* 1985) may be mediated by an unrelated mechanism such as alteration in the intestinal structure (Cassidy *et al.* 1981), intestinal enzyme profile (Farness & Schneeman, 1982), hepatic enzyme profile (Stanley & Newsholme, 1985) or peripheral sensitivity to insulin (Pederson *et al.* 1982).

Mixed nutrient combinations containing CS such as G + CS + CL and G + CS + CO + CL gave a significantly lower glycaemic response than G. This may be partly because these meals contained 60 g G instead of 100 g G. Another contributory factor might have been the insulinotropic effect of these combinations. The insulinotropic effect of proteins has been reported earlier (Berger & Vougaraya, 1966; Rabinowitz *et al.* 1966; Estrich *et al.* 1967; Flatt & Bailey, 1984) and has also been observed by us (A. Siddhu, S. Sud, R. L. Bijlani, M. G. Karmarkar and U. Nayar, unpublished results). But the present study also points to an insulinotropic effect of CL.

The mechanism of the insulinotropic effect of CL cannot be deduced from the present study, but it is possible that like G, CL also stimulates gastric inhibitory peptide (GIP) secretion from the duodenum, which in turn stimulates insulin secretion. This is not a very far-fetched suggestion because CL is a G polymer, and the terminals of its molecules may provide appropriate ligands for the same receptors which mediate the GIP-releasing effect of G.

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