

Part One

Nutrition and Health Considerations

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1 Glycaemic Responses and Toleration

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1.1 INTRODUCTION

Sugars and sweeteners have an important role in the human diet and choosing the right ones in the right amounts can influence health. Knowledge will enable good choices, and further research and understanding of the literature will confirm or deny how good our choices are, and where improvements are possible. Choice is not simply a matter of which is the healthier or healthiest, since the technological properties and economics of sugars and sweeteners impact on which of them can be used suitably in a particular food.

A wide range of potential influence on health is offered by sugars and sweeteners when selected appropriately, as will be evident in detail from other chapters. These include the following:

- A reduced risk of dental caries.¹
- Potential for improved restoration of the early carious lesions.²
- A reduction in caloric value that may contribute towards a lower risk of overconsumption, obesity and improved survival.^{3,4}
- Substrate for butyrate production, and potentially reduced risk of colon cancer.⁵
- The formation of osmolytes efficacious for laxation and lower risk of constipation or accumulation of toxic metabolites.⁶
- Substrate for saccharolytic and acidogenic organisms in the colon that contribute to prebiosis and 'digestive health' potentially including improved immunological function.^{7,8}

Each of these can influence the choice of sugars and sweeteners. Of particular relevance is their impact on glycaemic response and potential to contribute to low glycaemic index (GI) or glycaemic load (GL) diets.

Lowering post-prandial glycaemia and insulinaemia through an appropriate choice of sugars⁹ and sweeteners,⁷ together with other low-glycaemic carbohydrates,¹⁰ fibre, protein, lower energy intake and exercise,¹¹ can each improve glycaemic control. In turn, this appears to lower the prevalence or risk of developing metabolic diseases including metabolic syndrome, diabetes (and associated complications), heart disease, hypertension, stroke, age-related macular degeneration and certain cancers.¹²⁻¹⁶

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In those who are susceptible, lower glycaemic carbohydrate foods may also benefit appropriate weight gain during pregnancy,¹⁷ limit insulin requirements in gestational diabetes,¹⁸ potentially allow favourable foetal growth patterns and fat accretion,¹⁹ reduce neural tube defects²⁰ and aid recovery from surgery.²¹

Meta-regression of interventional studies of lower GI or GL diets show a time-dependent lower body weight over a 1-year period²² and supports weight maintenance after weight loss.²³ Reduced food intake in humans⁴ may be partly responsible for weight loss and maintenance. Lowering of body weight improves survival among newly diagnosed diabetes patients,²⁴ and may contribute to longer survival beyond old age as seen in animal studies while lowering glycaemia with isomalt.⁴

The converse of all aforementioned is that, given the right circumstances, a poor choice of type and amount of all carbohydrates, including sugars and sweeteners, could augment ill health. Attributes of sugars and sweeteners affecting health via the glycaemic response are nutritional and need to be seen in the context of the whole diet. It is appropriate, therefore, to consider the glycaemic aspect of diet and health from ancient to the present and future times – so far as these can be ascertained, explained and envisaged.

1.2 GLYCAEMIC RESPONSE IN ANCIENT TIMES

It is often argued that our genes might not cope with diets that are substantially different from those eaten by our ancestors.^{25–30} Quite what these diets were or how tolerant ancient genes have become are matters of uncertainty. Successful genes were in existence for both herbivorous and carnivorous diets prior to humankind; however, no early diet appears to have been high glycaemic. Those peoples who would normally consume ‘early’ or rudimentary diets, such as recent hunter–gatherers, experience low levels of diabetes and respond adversely to diets we may now consider high glycaemic.^{26,31} This is consistent with the notion that early genes were unadapted to high-glycaemic responses, and also consistent with a notion of adaptation having occurred in the people of today’s relatively more glucose-tolerant ‘western’ cultures, at least among a large proportion of them. Those not having adapted, contribute to prevalent diabetes and other conditions mentioned that are currently experienced, which is far higher than in either hunter–gatherers or rudimentary horticulturalists or simple agriculturalists or pastoralists.²⁶ For the people of these ‘basic’ cultures and for ‘unadapted’ westerners (easterners or southerners or northerners), a high-glycaemic response remains a health hazard, for which a variety of strategies exist to help them cope.¹¹ Europe has a rich culture and a documented history of its foods, and so we can obtain some idea of how the glycaemic character of diets may have developed over time.

Generally, we may assume diets to partly reflect the foods that can be found or are made available to eat. If this is so, examination of the inventory of foods identified in European history may shed some light on what was eaten and what might now be eaten for optimal health. Such an inventory is provided by Toussaint-Samat³² from which an assessment of the development in the glycaemia character of contemporary diets has been made taking account of the protein, fat, fibre and sources of carbohydrate (Figure 1.1). The picture cannot be accurate but what is clear is a progressive increase in the GL, with a markedly rapid increase in this GL following industrialisation. We cannot be sure of the prevalence of disease in Europe throughout the whole of this timescale, but we would not likely dispute that the prevalence of obesity and metabolic disease is as high now as ever.

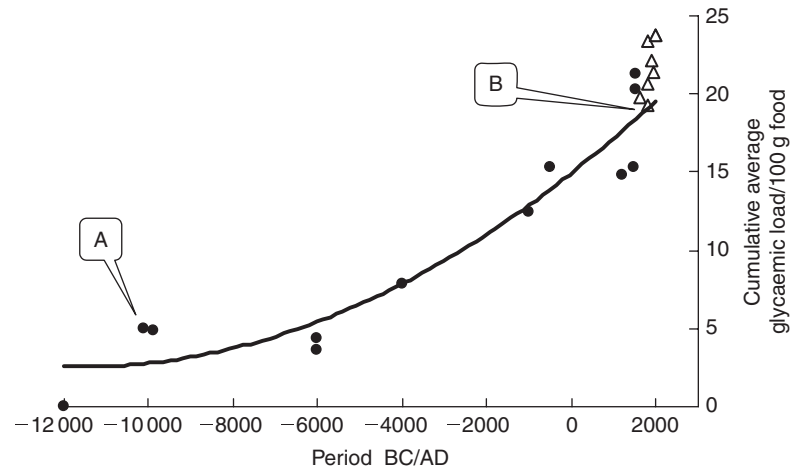


Fig. 1.1 Evolutionary adaptation to ancient diets of low glycaemic load may have left mankind genetically predisposed to non-communicable diseases provoked by today's high-glycaemic diets. Based on the history of foods in Europe,³² with calculations by this author (A, agricultural revolution; B, industrial revolution). Open symbols show values post the industrial revolution.

Such a trend is argued to also have occurred throughout more recent times in the United States,²⁵ with recent emphasis on reducing the fat content of the diet, a doubling of flour consumption during the 1980s and an increase overall in sugar, corn syrup and dextrose consumption prior to the end of the millennium.^{33–35} These together with a lower dietary fibre content of foods³⁴ imply exposure to diets eliciting a high-glycaemic response.

1.3 GLYCAEMIC RESPONSE APPROACHING THE MILLENNIUM

Much of our understanding of the interplay between health and the glycaemic response to foods has arisen from investigations into the dietary management of diabetes. Whereas very low-glycaemic carbohydrate foods such as Chana dahl were used in ancient India for a condition now recognised as diabetes,³⁶ nineteenth century recommendations in western cultures were for starvation diets, which were, of course, non-glycaemic. The drawback of such is obvious and in 1921, high-fat (70%) low-carbohydrate (20%) diets were recommended,³⁷ which by definition would be low glycaemic. A gradual reintroduction of carbohydrate into recommendations for diets for diabetic patients arose as carbohydrate metabolism came under some control using drugs, but mainly because 'dietary fat' was recognised to have a causal role in coronary heart disease, to which diabetics and glucose intolerant individuals succumb, more readily in some cases than others.^{38–41} The metabolic advantages of replacing dietary fat (saturated fat) with high-fibre high-carbohydrate was lower fasting glycaemia, lower total-, HDL- and LDL-cholesterol and lower triglycerides.^{42–46} Such benefits may in part be related to dietary fibre or its influence on the glycaemic response.^{47,48} Certainly, the non-digestible carbohydrate in these diets would ensure some degree of lower glycaemia for a given carbohydrate intake and support beneficial effects from lower saturated fat intake.

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During these times, the adverse influence of higher glycaemia or more dietary carbohydrate was either unrecognised or the risk was accepted by the medical profession in fear of (or compromise for) the adverse effects of 'dietary fat'. The adverse influence of higher glycaemia may also have been overlooked due to the apparent benefits of the non-digestible carbohydrate in the high-carbohydrate foods. Indeed, the Institute of Medicine has recommended high-fibre diets to combat coronary heart disease,⁴⁹ and this builds upon the dietary fibre hypothesis that proposed higher prevalence of diabetes, heart disease and other conditions associate with diets deficient of fibre.^{50,51} An absence of fibre in high-sugar products left sugar (sucrose) vulnerable; nevertheless, this sugar remained preferable among nutritionists to high (saturated) fat, which it might displace from the diet, giving rise to the concept of the 'sugar-fat-seesaw' discussed elsewhere.⁵²⁻⁵⁴

Throughout the whole of these times, the primary purpose of recommending energy from carbohydrate was to displace the intake of energy as fat. In part, this is because carbohydrate supplies energy, but also because carbohydrate counters the insulin desensitising influence of both mobilised body fat and dietary fat.⁵⁵⁻⁵⁷ This purpose for carbohydrate was retained in the GI concept, whereby carbohydrate of low-glycaemic response further improved glycaemic control in diabetes patients,¹⁰ and possibly the plasma lipid profile.⁵⁸

However, it must be considered whether carbohydrates have a long-term future as a means to displace fats from the diet. It is noteworthy that the increasing carbohydrate content of diets throughout European history, which partly explains the higher GL (Figure 1.1), has not adequately displaced 'fats' from the diet or prevented obesity. Excess of carbohydrate prevents the use of fat stores and encourages dietary fat to be stored. In general, elevating the consumption of monounsaturated and polyunsaturated (bar trans) fats is considered beneficial in respect of diabetes, coronary heart disease and a variety of conditions⁵⁹⁻⁶² and is consistent with early diets.⁶³ In addition, there is little or no evidence that carbohydrate ingestion can selectively limit the ingestion of saturated fats. Proponents of the Mediterranean diet (high in mono- and polyunsaturated fats) would hold that the use of carbohydrate for the purpose of limiting fat intake is unsound.

1.4 THE GLYCAEMIC RESPONSE NOW AND IN FUTURE NUTRITION

The general picture now for glycaemic control is that a high-fibre, low-glycaemic and low-saturated fat diet is optimal.⁶³ With obesity being a major problem and a risk factor for type-2 diabetes and heart disease, an appropriate energy balance has become of major importance.⁶⁴ Weight loss has for some time been recognised as important to the survival of newly diagnosed type-2 diabetes patients²⁴ and improvement in prognosis for cardiovascular disease.^{65,66} These are practical examples of how caloric restriction improves survival in at-risk groups. Of course, caloric restriction implies here a diet reduced in energy via lower saturated fat and lower GL than is generally consumed.

It is clearly preferable to limit the intake of both saturated fat and high-glycaemic carbohydrate as energy sources to facilitate weight reduction, rather than simply to exchange energy sources. Prior nutritional debates of 'fat versus carbohydrate' might now be viewed as too imprecise in both the description of the food components and how the components are pitched against each other. A similar concern arises when it is argued that low-GI foods should find automatic favour over low-GL foods when in communication with the consumer.

Choosing low-GI foods does not automatically mean maintaining a lower fat intake since approximately 50% of the variance in the GI of foods can be attributed to their fat content. The nutrition debate still needs to provide greater scope for consideration of the adverse influence of 'saturated fats *plus* high-GL' together in general nutrition.

Sugars and sweeteners provoke a range of glycaemic responses related to the carbohydrate structure without the need to ask whether the glycaemic response is actually brought about by co-ingested dietary fat,^{7,9,67} and so may variably promote, defer or help prevent ill health. Various research groups indicate at the time of writing that 'the concepts and methods regarding the GI [or GL] are sufficiently mature to recommend preparing the population to use GI as a way to help choose healthier foods...'¹⁶ This is a position consistent with that over a decade ago in the WHO/FAO recommendations to primary producers and processors of foods: 'Consider how existing and new technologies can be used to help meet dietary goals regarding the quantity and nutritional properties of food carbohydrates...' and to 'provide appropriate information to the consumer on food labels.'⁶⁸

1.5 GLYCAEMIC RESPONSE AND ADVERSE OUTCOMES: BOTH PHYSIOLOGICAL AND IN RESPONSE TO ADVICE

Advice to consume a diet of low-, in exchange for high-glycaemic foods has raised consideration about whether this would detract from other nutritional advisory messages. There are, however, no known adverse effects of choosing a diet including low-glycaemic carbohydrate foods instead of high-glycaemic ones,⁶⁹ other than for occasionally temporal gastrointestinal discomfort whenever this is accompanied by excessive low digestible carbohydrate ingestion (discussed in Section 1.10).

Occasionally claims are made that the benefits of low GI can be achieved by selecting whole grain foods, fruits and legumes, and that low-glycaemic advice would interfere with this whole food advice. However, such benefit of whole foods is hardly ever likely to be achieved optimally because the glycaemic indices of foods in these food categories cover wide ranges of GI values (Figure 1.2). Intervention choosing low instead of high-GI fruits is shown to be of benefit to diabetes patients, for example.⁷⁰

1.6 MEASUREMENT AND EXPRESSION OF THE GLYCAEMIC RESPONSE

By 1929, the potential of carbohydrate to raise plasma glucose, some of which may spill over into urinary losses in diabetes patients, was indicated by its available carbohydrate content,⁷¹ for which a direct assay to determine the composition of foods was later refined.⁷² Fibre was suitable for diabetes patients as it provided no glucose, to either elevate plasma glucose concentrations or urinary losses. Another measure of the glycaemic potential became known as the GI.⁷³ Later, the quantity called GL, the product of available carbohydrate and GI, was introduced⁷⁴ and validated as a measure of the glycaemic response.⁷⁵ GL can be assayed directly and without need for knowledge of the available carbohydrate content,⁷⁵⁻⁷⁷ about which assumptions are too often made.⁴ The GI became widely known, and many GI testing centres have opened. Meanwhile, GI has received criticism as it is said to not meet

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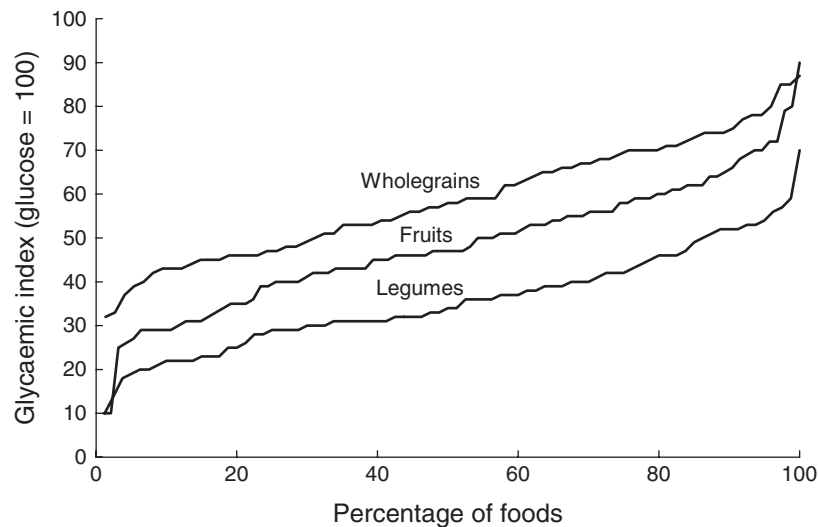


Fig. 1.2 Wholegrain, fruit and legume foods each span a wide range of glycaemic index (GI) values. Information is on 74 wholegrain food, 94 fruit foods and 80 legume foods from the 2008 International Tables of GI and glycaemic load,⁷⁹ and are presented in order from the lowest to the highest GI.

many useful criteria for inclusion in conventional food tables or in communication with the consumer,⁷⁸ though tabulation is possible and finds application nonetheless.^{67,79}

The precision of the GI assay, initially examined in a study among five laboratories based on capillary blood sampling using high-carbohydrate foods,⁸⁰ has since been the topic of discussion with the aim of standardisation,⁸¹ has subsequently been assessed among 28 different laboratories,⁸² and now has Australian⁸³ and International⁸⁴ standardisation. The standardised protocol is only a little different now from that used in the first inter-laboratory study in particular, with regards to the precision achieved. An outstanding question is whether the methods for assessing GI and GL are adequately reproducible for communication with the consumer.

A useful point of reference when assessing a method's adequacy is one often used in regulatory enforcement for substantiation of reported or declared values in food labelling. Tests need to be able to assess whether a reported value is compliant with regulations specifying boundaries of accuracy required for labelling purposes. Such enforcement often finds it generally practical to 'accept' an 'error' of no more than 20% in a nutrient value reported on a food label in comparison with an officially analysed (or assessed) value.⁸⁵ Such an apparently large 'permitted' discrepancy ensures that differences between reported and official values do not arise simply by chance due to imprecision of the test method. However, this particular approach of using a nutrient value as the reference amount that defines the absolute size of the 20% value has limitations. One is that the 20% of nutrient value is extremely onerous when nutrient values are low, because as the value approaches zero, the percentage error approaches infinity. The second is that the 'permissible error' differs according to the nutrient amount; 20% of 1 g is 0.2 g, but 20% of 100 g is 20 g, which is 100 times higher. The third is that a constant 20% of nutrient value fails to follow the real error structure in the analytical data except if the error size is an exact proportion of the measurement size, which for biological tests is practically never. For a test such as GI, a basal

Table 1.1 Precision of glycaemic response^a values according to the definition of the 'true' value.

Sucrose and alternatives	Glycaemic response (g GL/100 g ingredient) ^a	LSD from 'true' value (g GL/100 g ingredient) ^b	
		Definition a (true = single laboratory result) ^c	Definition b (true = combined laboratory results) ^d
Sucrose	64	11	4
Erythritol	0	5	2
Xylitol	12	10	4
Sorbitol	9	7	3
Maltitol	45	12	4
Regular maltitol syrup	52	14	5
Isomalt	9	9	3
Lactitol	6	6	2

GL, glycaemic load; LSD, least significant difference.

^aExpressed as glycaemic load (g equivalents of glucose per 100 g carbohydrate ingredient) as would be derived using the glycaemic index protocol. The value and standard deviations of reproducibility are estimated for data on sucrose from ref. 79 and data on alternatives are from ref. 7.

^bLSD; least significant difference between claimants analysis and the 'true value' at $P < 0.01$.

^cThe true value being that defined as true according to results from a single proficient assessment laboratory and testing of the difference in analyzed values $A - B$ from the claimant and assessment laboratory value, respectively.

^dThe true value being that defined as true according to results combined from the two laboratories involved; that is from an assessment laboratory and from a laboratory providing an original value the source of information declared on a label, and so testing the difference $A - (A + B)/2$.

or zero response does not have zero error of measurement. For a biological test, the 20% of nutrient value, if invoked, would not therefore seem to be a practical tool for assessment of compliance of a nutrient value with potential regulations – as noted previously in the first edition of this book⁸⁶ and now elsewhere.^{87,88} Rather, some other reference amount would seem useful as used, for example, with vitamin C or iron for which dietary reference values (DV) can provide the reference amount, that is something other than a nutrient value can be used as reference amount.

On the basis of the data from inter-laboratory studies^{80,88} and the composition of foods,^{82,89} the GI methodology may appear difficult to justify from an analytical perspective alone because of its imprecision among laboratories (Figure 1.3). By contrast, this is less apparent for GL (Figure 1.3), making GL a potentially suitable measure or method of expression of the glycaemic response for communication with the consumer.

This conclusion for GL applies also to sugar and alternative sweeteners (Table 1.1) whether or not GL is expressed per 100 g available carbohydrate (e.g. the GI of sucrose) or per 100 g ingredient weight for the alternative bulk sweeteners so far examined. The difference in accuracy between GI and GL (Figure 1.3) arises simply because of the different reference amounts: 100 g carbohydrate in the case of GI (expressed g GL per 100 g carbohydrate = GI), and 100 g fresh weight of food product or ingredient in the case of GL (expressed as g GL per 100 g fresh weight). The 100 g fresh weight might equally be substituted by 100 g GL, where ~100 g GL per day (or per 2000 kcal) might be optimal for prevention of metabolic conditions such as coronary heart disease or type-2 diabetes and possibly other diseases (Livesey and Taylor, unpublished observations, 2008).

A further issue with regard to compliance is that of defining the true value with which the reported or claimed nutrient value (GI or GL) should comply. One possibility (definition 'a')

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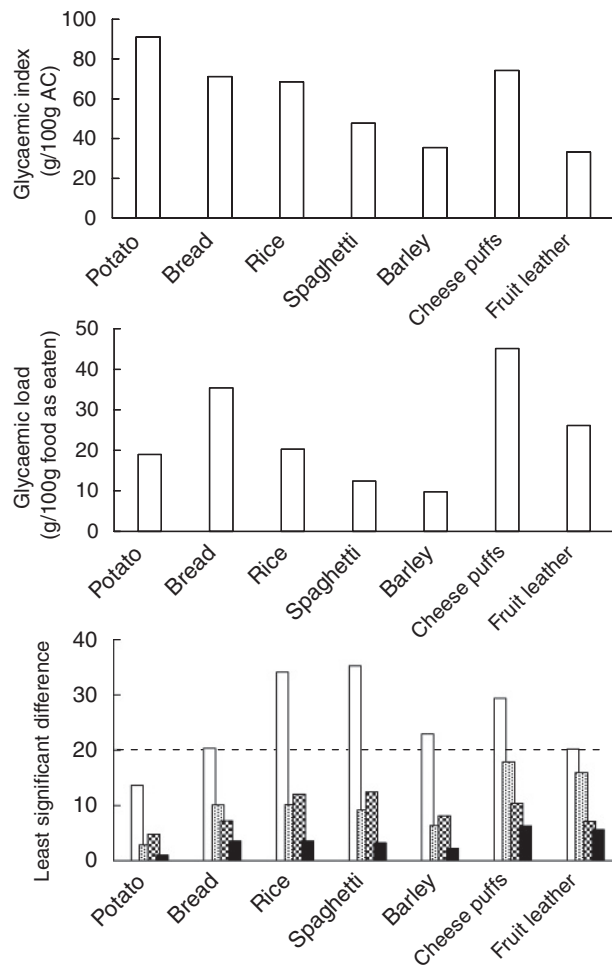


Fig. 1.3 Precision of measurement and expression of the glycaemic response. Data are based on inter-laboratory studies^{80,82} and the composition of these foods.^{82,89} The least significant difference (LSD) is either (a) the size of difference between a claimant laboratory value and a subsequent assessment laboratory value or (b) the size of difference between a claimed value and the true value; the last being the combined mean of the claimed and the subsequently assessed values, assuming both laboratories are proficient. $LSD = t \times SD_{\text{reproducibility}}$ (standard deviation of reproducibility) for $p < 0.01$ and t is approximated by the multiplier 2.8 as described in ISO standard 5725.¹⁴⁰ The validity of this approach implies that $SD_{\text{reproducibility}}$ is the apparent among laboratory standard deviation, apparent because it combines the within laboratory and the true among laboratory variabilities (and any interaction). The four bars from left to right: GI by definitions 'a' and 'b', and GL by definitions 'a' and 'b'.

in the legend to Figure 1.3) is that the analysed value provided by an assessing laboratory is considered the true value. However, this is problematic if both reporting and assessing laboratories are proficient because scientific validity would favour a combined value for the two laboratories as defining the true value. In this case, the between laboratory standard deviation would be smaller by $1/\sqrt{2}$ (definition 'b' in the legend to Figure 1.3) and the difference between the true value and the claimant laboratory value would be half that for the

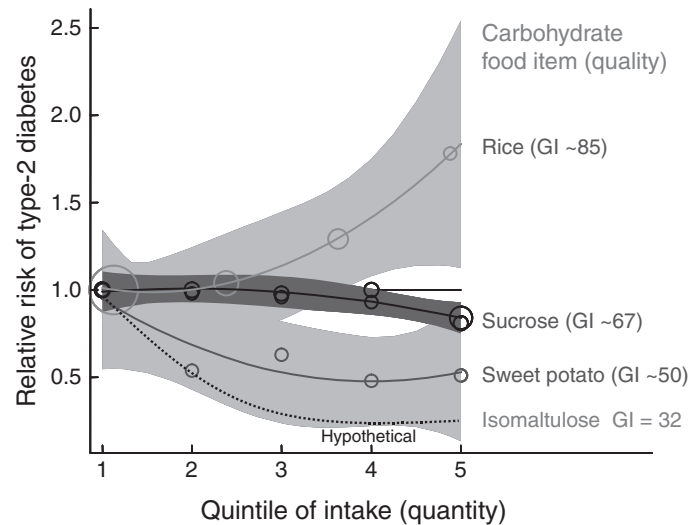


Fig. 1.4 Both the quantity and quality of carbohydrate food affect the relative risk of type-2 diabetes. Relative risk data are from large prospective observational studies for rice and sweet potato¹⁴¹ and sucrose.^{116,142} The hypothetical curve for isomaltulose is hand drawn based on its glycaemic index of 32 (Table 1.2). Shaded areas are 95% confidence intervals. Originally published at the Diabetes UK Annual Professionals Conference, Glasgow, March 2008.¹⁴³

difference between the values obtained by two laboratories (all assuming both laboratories reach a similar precision). Using definition 'b', now both GI and GL might be considered sufficiently precise for communication with the consumer at a 20% level of compliance, while GL might be considered suitable at a compliance level of 10%.

In considering the foregoing, readers should be aware that there is at present no international consensus of whether GI or GL (or other approach to assessing glycaemic response) is a preferred measure for communication with the consumer, though local preferences worldwide appears to favour GI. Nor is there international consensus on the approach that should be taken for assessing compliance. Nevertheless, scope evidently exists for regulatory procedures to facilitate the communication.

In considering the choice between GI and GL as the expression for communication, consideration might also be given to prospective observational studies (Figure 1.4), which illustrated the following:

- Both the quantity and the quality of carbohydrate food or ingredient affect the risk of type-2 diabetes.
- Carbohydrate such as sucrose with a middle-of-the-road GI appears to not affect the relative risk of type-2 diabetes. Thus, also total carbohydrate, which has a middle-of-the-road GI, would not be expected to affect the diabetes risk in prospective observational studies.
- Replacement of a high-glycaemic starch staple with a low-glycaemic starch staple would lower the relative risk of type-2 diabetes.
- Although sucrose appears without effect on the relative risk of type-2 diabetes, hypothetical considerations suggest its replacement by an alternative carbohydrate such as isomaltulose of lower GI (Table 1.2) has potential to lower the relative risk.

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Table 1.2 Glycaemic and insulinaemic responses to bulk sweeteners and alternatives.

Sugars or alternatives	Relative glycaemic response (RGR)	Categorisation (high, intermediate, low, very low)	Relative insulin response (RIR)	Citation
<i>Starch hydrolysis products</i>				
Maltodextrin	91	High	90	<i>a, b</i>
<i>Disaccharides</i>				
Maltose	105	High	–	<i>c</i>
Trehalose	72	High	51	<i>d</i>
Sucrose	68	Intermediate	45	<i>c, d</i>
Lactose	46	Low	–	<i>c</i>
Isomaltulose	32	Very low	27	<i>a</i>
<i>Monosaccharides</i>				
Glucose	100	High	100	<i>d</i>
Fructose	19	Very low	9	<i>d, c</i>
Tagatose	3	Very low	3	<i>a, e</i>
<i>Hydrogenated monosaccharide</i>				
Erythritol	~0	Very low	2	<i>d</i>
Xylitol	12	Very low	11	<i>c, d</i>
Sorbitol	9	Very low	11	<i>d</i>
Mannitol	~0	Very low	~0	<i>d</i>
<i>Hydrogenated disaccharides</i>				
Maltitol	45	Low	27	<i>d</i>
Isomalt	9	Very low	6	<i>d</i>
Lactitol	5	Very low	4	<i>c, d</i>
<i>Hydrogenated polydispersed saccharides</i>				
Maltitol syrup				
High maltitol	48	Low	35	<i>d</i>
Intermediate maltitol	53	Low	41	<i>d</i>
Regular maltitol	52	Low	44	<i>d</i>
High polymer	36	Very low	31	<i>d</i>
Polyglycitol	39	Very low	23	<i>d</i>
Hydrogenated polydextrose	~5	Very low	~5	<i>c</i>
<i>Non-digestible polysaccharides</i>				
Polydextrose	~5	Very low	~5	<i>c</i>
Resistant maltodextrins	~10	Very low	~10	<i>f</i>
Fructans	~5	Very low	~0	<i>g</i>

RGR, relative glycaemic response (% of that for oral glucose); RIR, relative insulin response (% of that for oral glucose).

^aSydney University Glycaemic Index Research Service.

^bMacdonald and Williams¹⁴⁶ in article entitled 'Effects of ingesting glucose and some of its polymers on serum glucose and insulin levels in men and women'.

^cFoster-Powell et al. and Atkinson et al.,^{67,79} in articles on 'International table of glycaemic index and glycaemic load'.

^dLivesey⁷ in article entitled 'Health potential of polyols as sugar replacers, with emphasis on low glycaemic properties'.

^eDonner et al.⁹⁷ in article entitled 'D-tagatose, a novel hexose: acute effects on carbohydrate tolerance in subjects with and without type-2 diabetes'.

^fOhkuma et al.¹⁴⁷ in article entitled 'Pyrolysis of starch and its digestibility by enzymes'.

^gRumessen et al.⁹⁸ in article entitled 'Fructans of Jerusalem artichokes: intestinal transport, absorption, fermentation, and influence on blood glucose, insulin, and C-peptide responses in healthy subjects'.

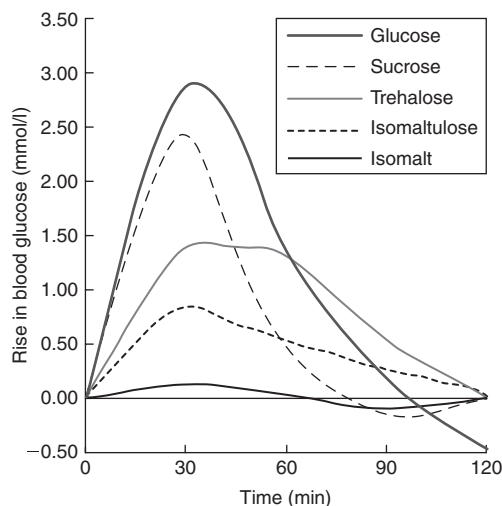


Fig. 1.5 Potential now exists to tailor the glycaemic response of sweetened foods by choosing ingredients. The response curves shown are for 50 g ingredient, relative to glucose in healthy people. Information on other low-glycaemic sweeteners and bulking agents is given in Table 1.2 together with references.

1.7 THE ACUTE GLYCAEMIC RESPONSE TO SUGARS AND ALTERNATIVES

The acute glycaemic response to glucose, sucrose, trehalose, isomaltulose and isomalt (Figure 1.5) illustrate how it is now possible to create bulk sweeteners, and so tailored foods, with almost any glycaemic response, likewise the insulin response (not shown). Other examples together with insulin responses are summarised in Table 1.2.

A numerical value for GI or GL does not itself provide information about whether the values are high or low compared with the range for foods eaten or compared with diets that associate prospectively with the incidence of disease or death. To put information about the glycaemic response of foods into perspective, the GI has been classified according to whether it is high, intermediate, low or very low⁷ (www.glycaemicindex.com), as shown in Table 1.3. This classification may also help to communicate with the patient or consumer. For example, it can be suggested that a consumer or patient selects food from a lower band of glycaemic response (i.e. lower class or two lower classes where possible). Further, should a

Table 1.3 Classifications of glycaemic index (GI) and glycaemic load (GL).

Glycaemic classification ^a	GI ^b (g eq./100 g)	GL ^c (g eq./day)	GL ^d (g eq./serving)
High	>70	>120	>20
Intermediate	>55–70	>80–120	>10–20
Low	>40–55	>20–80	>4–10
Very low	0–40	0–20	0–4

^aBased on www.glycaemicindex.com and ref. 7.

^bBased on measurements with 25–50 g carbohydrate.

^cBased on prospective epidemiology.^{74,115–117}

^dBased on a 10 g serving size (or exchange rates) noted in the international tables.^{67,79}

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high-glycaemic food be eaten at a meal for any reason (e.g. enjoyment) any other carbohydrate source eaten at the same time ought to come from a low-glycaemic band. Furthermore, diabetes patients have for years practiced carbohydrate exchange as part of dietary therapy, for which a similar glycaemic response or similar insulin requirement was (and sometimes still is) presumed to arise from any food containing 10 g of carbohydrate. Diabetes patients can now update this approach by practicing exchanges based upon the GI or GL, while also attempting to reduce saturated fat intake. The alternative may be emphasised, limit energy intake while still eating (or eating more) low-glycaemic carbohydrate and mono- or polyunsaturated fats. Some advantages of the GL over the GI have been emphasised.^{4,78} Thus, GL can be used as a 'virtual nutrient' to be considered alongside all other nutrients when assessing the relation between diet and health.

The indication that GL should be limited to 120 g per day (Table 1.3) implies some 40–60% of people in western populations may be at risk of metabolic disease; this is consistent with the high prevalence of coronary heart disease, obesity and diabetes.

Intense sweeteners are consumed in such small quantities that they have no glycaemic response of their own; additionally, the structure of such sweeteners would normally not be expected to yield glucose upon metabolism. Generally too, none of the intense sweeteners have pharmacological actions to improve glycaemic control (an exception is stevioside⁹⁰). Aspartame is a more typical example of an intense sweetener that is without acute glycaemic response,^{91,92} another is sucralose.⁹³ Clearly however, compared with maltodextrins, maltose, glucose and sucrose, under controlled conditions marked reductions in the acute glycaemic response would be expected for intense sweeteners delivering comparable sweetness. Addition of intense sweeteners to foods or drinks that normally would not contain sugars for sweetness would, however, confer no glycaemic advantage.

The use of intense sweeteners in place of glycaemic carbohydrates wherever bulk is necessary for technological or organoleptic reasons requires the glycaemic response to bulking agents to be considered here too. The glycaemic (and insulinaemic) response to maltodextrin, bulk sweeteners and bulking agents varies considerably (Table 1.2). The causes of the lower glycaemia are numerous.⁷ Compared with glucose, the lower value for sucrose is due mainly to dilution within the molecule with a fructose moiety. A similar situation occurs with maltitol, maltitol syrups and polyglycitol, where glucose moieties are 'diluted' with a sorbitol moiety. Fructose alone is low glycaemic due to both slow absorption and need for conversion to glucose in the liver prior to appearance in blood as glucose; in addition, the carbohydrate may be partly stored as glycogen rather than released into the circulation. Further still, the energy from fructose is conveyed in the circulation for oxidation in part as lactate more than is the case for glucose. A similar situation occurs for sorbitol and xylitol, though slower absorption likely gives rise to less lactate; in addition, a high proportion escapes absorption. With isomalt and lactitol, an even greater proportion escapes absorption, which gives these polyols the lowest glycaemic response of all so far mentioned. Another polyol, erythritol, is almost unique in that although most is absorbed, it is low glycaemic; this is because it is poorly metabolised in the tissues and is excreted in the urine. Mannitol behaves similarly, though is largely (75%) unabsorbed.

At the other end of the scale are maltodextrins, which can give rise to a glycaemic response as high as glucose, likewise maltose. Trehalose, an isomer of maltose, has a glycaemic response comparable to sucrose (Table 1.2) in terms of its GL (g glucose equivalents per 100 g), though it peaks less sharply and there is persistence in the raised glycaemia that would likely help protect against hypoglycaemia in susceptible individuals. Isomaltulose, derived by rearrangement of sucrose, gives a similar though lower profile, and so lower GL;

this even though all of the isomaltulose is hydrolysed and absorbed. Other low-glycaemic carbohydrates include tagatose, fructans (fructo-oligosaccharides and inulin), polydextrose and resistant maltodextrins. The reduction in glycaemia caused by sucrose replacing high-glycaemic starch is considered an advantage.⁹ Greater reductions would be possible on replacing maltodextrin, maltose, glucose and sucrose with alternative sweeteners, either partially or completely depending on the serving size of foods.

Among the studies undertaken with polyols (mainly with maltitol, isomalt and sorbitol), the glycaemic response versus glucose is similar in people with normal and abnormal carbohydrate metabolism, as exemplified by type-1 and type-2 diabetes patients, provided insulin-dependent participants receive insulin via an artificial pancreas.⁷ This is as experienced with carbohydrate foods generally.⁶⁷ This similarity of GI between disease states, however, may not extend to similarity in the insulinaemic index between states.⁹⁴

In addition to having lower glycaemic responses, polyols, low-digestible sugars and bulking agents can reduce the glycaemic response to other carbohydrates. The magnitude of this effect is not great, but is not insignificant either and is in the order of 10–15%.^{7,95–97} However, no such effect is reported with fructans.^{98,99} The important conclusion here is that the low-glycaemic character intrinsic to these carbohydrates is not lost when they are consumed with other carbohydrates (or other macronutrients).

A further reduction in acute post-prandial glycaemia can occur when fat is included in the meal. This is common to both digestible and non-digestible carbohydrate whether used as sweeteners or not.⁷ It is accompanied by an elevation of insulinaemia via an incretin response. A common view is that fats reduce glycaemia via stomach emptying, however, this would not explain the elevated insulin response; thus, both stomach emptying and a gastrointestinal incretin response contribute to the lower glycaemia. The implications of the elevated insulinaemia in such a circumstance remain to be researched. However, sugar–fat mixtures (and more generally, high-glycaemic carbohydrate–fat mixtures) are not viewed as beneficial and too high an insulin response may contribute to the development of obesity¹⁰⁰ and coronary heart disease.¹⁰¹ Hence, it may be particularly important to reduce the glycaemic response of fatty foods (and the fat content of high-glycaemic foods). In this respect, this author notes the beneficial impact of low-glycaemic foods on long-term glycaemic control in diabetes patients appears greater among consumers of moderate- (35–40%) rather than low-fat (25%) diets.

A question arises as to whether sweeteners affect the cephalic phase insulin response (i.e. do sweeteners cause an elevation of insulin and so lowering of glycaemia, reflexively via the brain?). This appears not to happen to a significant extent with the sweeteners aspartame or saccharine.^{92,102} Likewise, in diabetic patients, sweetness is reported to have no impact on food intake and macronutrient composition other than perhaps for a lowering of sucrose ingestion.^{103,104}

1.8 LONG-TERM GLYCAEMIC CONTROL WITH SWEETENERS AND BULKING AGENTS

Fructosamine and glycated haemoglobin (HbA_{1c}) in blood are medium and long-term markers of day-long exposure to elevated blood glucose concentrations. Non-, pre- or undiagnosed diabetic individuals as well as diabetes patients with elevated HbA_{1c} are at increased risk of coronary heart disease, stroke and all cause mortality.^{105–107} In diabetes patients, the elevation

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of HbA_{1c} is associated also with higher risk of retinopathy, nephropathy, perivascular disease, limb amputation and perivascular deaths.^{105,107,108} While markers of risk for cardiovascular disease in interventional studies have usually been limited to lipid markers, it is recognised that good glycaemic control is of first importance in the control of diabetic hyperlipidaemia.¹⁰⁹ Possibly, glycated protein markers are underutilised as a tool to assess risk to health in both epidemiological and interventional studies. Mechanisms of increased risk are discussed elsewhere,¹¹⁰ and indicate greater risk whenever anti-oxidant defences are low.

Of all the risk markers used often in intervention studies with diabetes patients, only fasting blood glucose, fructosamine and HbA_{1c} show a consistent improvement, either in direction alone or in both direction and statistical significance due to replacement of high- with low-glycaemic carbohydrate foods.^{10,45} It should not go unrecognised that replacement of saturated fat with high-fibre high-carbohydrate diets also improves fasting blood glucose (total cholesterol and triglycerides) in type-2 diabetes patients, and a role for non-digestible carbohydrate in this response is evident.⁴³

This risk to glycaemic control from high-glycaemic carbohydrate in type-2 diabetes is reduced by the use of several substrates in place of carbohydrate, including protein,¹¹¹ the polyol isomalt⁷ and fructose^{112,113} as well as low-glycaemic carbohydrate foods.^{10,45} The implication is that it is the size of the overall glycaemic exposure in response to foods that associates with risk; this is more than simply explainable by GL, and GL more than GI, as noted previously.⁴ This hierarchy requires careful understanding. Here, high (saturated) fat diets elevate the glycaemic response to foods chronically via deterioration in insulin sensitivity and beta-cell function, so amplifying the glycaemic response to carbohydrate foods rather than by supplying fuel for blood glucose formation. In essence, both saturated fat and high-glycaemic carbohydrate each pose a risk to glycaemic control and health. Additionally, both add energy to the diet, so potentially contributing directly to the obesogenic environment.

A further consideration is that when study participants already have good glycaemic control, then only two outcomes are possible by change of diet, either no effect or deterioration, which may take years before overt disease emerges. A third possibility arises when glycaemic control is poor; it may improve within weeks and months. This is evident (in the author's assessment) for mixed groups of type-1 and type-2 diabetes patients, for whom intervention with low-glycaemic carbohydrate diets seem most effective in people with poor glycaemic control. In such studies, poor glycaemic control associates in the first instance with moderate- rather than low-fat ingestion.

Based on the available evidence from intervention studies, low-glycaemic diets will correct about 30% of the deterioration in glycaemic response (author, unpublished), which implies an approximately 30% reduced risk of diabetic complications and heart disease.¹¹⁴ Interestingly, when looking at initially healthy people via prospective epidemiological studies, high- versus low-GL diets appear to explain about 30–40% of the relative risk for type-2 diabetes^{74,115,116} and perhaps more of cardiovascular disease, in women especially.^{14,117} Interestingly too, use of an inhibitor of carbohydrate digestion in a pre-diabetic state can reduce the incidence of coronary heart disease by up to 50%.¹¹⁸ How much more effective life-long exposure to low-glycaemic diets would be in current inactive societies remains uncertain – though prospective studies of 20 years duration suggest possibility of greater benefit than those of 5–6 years duration.^{119,120} On the basis of such data, there would appear to be a significant public health benefit from minimising high-glycaemic carbohydrate consumption. It is reasonable, therefore, for food manufacturers to begin or continue to consider how they can either replace or minimise either high-glycaemic carbohydrate and saturated fats or both in foods, and in this sugars and sweeteners have a role.

Few recent studies have examined the impact of polyols. One study examined the influence of isomalt on both fasting and post-prandial plasma glucose and glycated haemoglobin in diabetes patients, showing improvement in all three parameters¹²¹ as shown by the author's analysis of original tabulated data.⁷ The isomalt was consumed in such a way that it was likely to have reduced the intake of sucrose. In healthy people, by contrast, isomalt appears to have no influence on fructosamine concentrations. Again, this is consistent with studies of other low-glycaemic carbohydrate foods, where severity of the disease condition impacts on the magnitude of effect.

Replacement of sucrose with fructo-oligosaccharides (<10 g per day) caused a relative reduction in fasting glucose in type-2 diabetes patients over 14 days by 10% in one study,¹²² and by 6% in another when exchanging 20 g sucrose with fructo-oligosaccharides for 4 weeks. By contrast, no similar influence occurred in people without diabetes.^{123–126} This is consistent with the lower glycaemic impact of fructans compared with sucrose. Such a result again mirrors an improvement in glycaemic control in diabetes patients but not persons with normal blood glucose concentrations when replacing high- with other low-glycaemic carbohydrate foods.²² However, small shifts in glycaemic control away from the healthy normal appear partially correctable with low glycaemic carbohydrates that undergo fermentation (see Section 1.9).

The chronic effect of D-tagatose on blood glucose is unclear.¹²⁷ As might be predicted, no influence was seen on fasting blood glucose in normal individuals over 8 weeks. In eight diabetes patients, feeding supplemental tagatose had no effect on plasma glucose or HbA_{1c}, though the study was under-powered and it is unclear whether GL was significantly reduced. Supplementation with a similar amount of glucose would almost certainly have damaged glycaemic control.

Randomly bonded glucose (polydextrose) had no influence on glycaemic control (HbA_{1c}) in normal subjects,¹²⁸ but 20 g daily (resistant maltodextrin) reduced fasting glucose in type-2 diabetes patients,¹²⁹ again consistent with expectations with low-glycaemic carbohydrate foods. Carbohydrates such as these may well be corrective and preventive, neither of which can occur in fully healthy persons, and which in non-diabetic individuals (blood glucose >5 and <7 mmol/l) is hard to identify without combining information from many studies.¹³⁰

Given that reduction of dietary (saturated) fat and high-glycaemic carbohydrates will each lower HbA_{1c}, it is not surprising that using a mixture of non-digestible carbohydrate and intense sweetener as a fat replacer should contribute to lower HbA_{1c} concentrations in diabetes patients.¹³¹ Again, this observation plus those mentioned previously lead to the conclusion that improvement in glycaemic control arises from both a lower ingestion of saturated fat and the consumption of low-glycaemic carbohydrate including sweeteners and bulking agents in preference to high-glycaemic counterparts. However, intense sweeteners alone added to a diet may have little or no direct influence on long-term glycaemic control, as shown with aspartame.^{93,132} Note, however, improvement in glycaemic control would be difficult to establish in individuals without diabetes within a period of a few months¹³³ or in diabetes patients in whom control was already well established, again within a period of a few months.¹³⁴ Benefits for individuals at risk of diabetes, hypertension and coronary heart disease may take years to develop as shown using pharmacological approaches to reducing post-prandial glycaemia.¹³⁵

The observations to date support the view that sweeteners with a combination of low-glycaemic response and reduced energy value can contribute to an environment in which obesity, diabetes and potentially coronary heart disease and certain cancers are less likely to develop.

1.9 ARE LOW GLYCAEMIC CARBOHYDRATES OF BENEFIT IN HEALTHY PERSONS?

In short, the answer appears to be yes, and while it is unclear whether this means yes in all healthy persons or just a good proportion of healthy persons who would progress to metabolic disease and associated cancers remains to be established:

- Meta-analyses of prospective observational studies on populations of healthy persons suggest both low GI and low GL, especially when coupled with high unavailable carbohydrate content, lowers the risk of diabetes, cardiovascular disease, age-related macular degeneration and certain cancers in persons with no established disease at the outset of study.^{16,136}
- Meta-analysis of interventional studies in groups of persons with varied severity of glycaemic control shows both low GI or GL and high unavailable carbohydrate content partially corrects departures from normal of glycaemic control at all levels from near normal to moderate diabetes.²²
- Meta-analysis of interventional studies that lower the acute glycaemic response of available carbohydrate, by way of introducing an unavailable carbohydrate to the diet for 3 months, can partially correct fasting blood glucose in healthy persons with fasting glucose >5 mmol/l and pre-diabetic as well as in diabetic individuals.¹³⁷
- The potential relevance of low-glycaemic carbohydrate, as outlined by WHO/FAO⁶⁸ and ILSI NA¹⁶ leads to the conclusion that low-glycaemic response assess either as GI or GL is now 'sufficiently mature' to apply in communications with the consumer.

1.10 GASTROINTESTINAL TOLERANCE IN RELATION TO THE GLYCAEMIC RESPONSE

The topic of gastrointestinal tolerance has been considered in detail elsewhere.^{6,138,139} Here consideration is given to the impact of intolerance on the capacity for GL reduction by exchange of sugars, sweeteners and bulking agents, selecting examples to illustrate some key points. Thus the greater the amount of carbohydrate that is exchanged the greater the GL reduction that is possible; this is until people consuming the alternative carbohydrate turn away due to gastrointestinal intolerance, as indicated in Figure 1.6. For this purpose, intolerance is assessed from the proportion of people in sampled populations that experience mild watery stools after alternative carbohydrate ingestion. This proportion is summarised according to a model with binomial distribution that can be described by two parameters: one is the highest dose at which no response is observed by any individual in the population sample (threshold, D_0) when intake is in divided doses, and the other is the sharpness of the response (S) as the dose is increased further. In the realistic range of intakes in divided doses up to 50 g daily both polydextrose and isomalt are well tolerated in adults, allowing considerable advantage in GL reduction to be gained from carbohydrate exchange. Although maltitol is well tolerated, its glycaemic response is the highest so that it gains less in terms of GL reduction up to the threshold. Fructo-oligosaccharide, which has a low-glycaemic response, is evidently least well tolerated, and this limits its potential for reduction of GL. Data such as these are essential when examining risk and benefit of alternative carbohydrates. The outcomes illustrate, in addition to the potential for GL reduction, that polyols are not

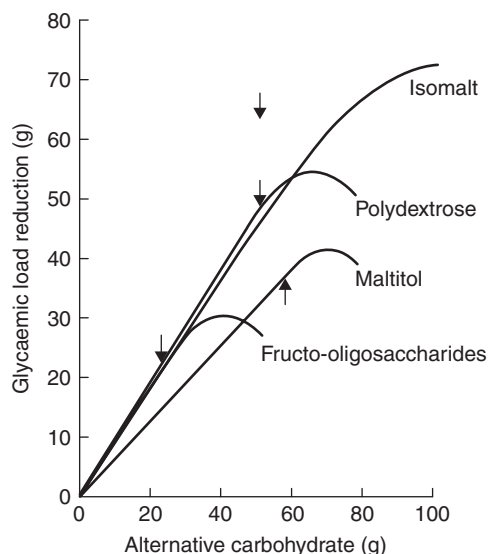


Fig. 1.6 This shows the balance of glycaemic load reduction and gastrointestinal intolerance for selected alternative carbohydrates. The curves are based on the author's unpublished analysis of information from the literature on tolerance^{6, 138, 144, 145} and glycaemia (Table 1.2). The arrows indicate thresholds of tolerance.

inevitably more laxative than oligo- and polysaccharides. The latter suggests that laxation is dependent on the fermentation process as much as the amount of fermentable carbohydrate and its molecular weight. Erythritol, another polyol, is not without effect on gastrointestinal tolerance, though it is well tolerated owing to it being mostly absorbed. It is as effective at GL reduction as isomalt and polydextrose up to 50 g intake daily in divided doses. The magnitude of such reductions alone are of potential public health and clinical importance and would certainly contribute to reductions managed by carbohydrate exchange in the diet as a whole;⁷ especially as some individuals are capable of tolerating considerable amounts of these carbohydrates, well above population threshold values.

1.11 CONCLUSION

While non-communicable diseases are set to overburden private and governmental health budgets, there is need of preventive methods to maintain health. Dietary change provides one such method and specifically reducing the glycaemic response to diet via food selection, food modification and ingredient choices and development is a valuable objective. There is now growing evidence from clinical data confirming the potential for reduced severity of disease, and from epidemiological data for reducing the risk of developing a variety of non-communicable diseases. Incorporation of the low-glycaemic approach as one component of a 'better diet' is likely to remain important. Strategies that combine reduced GI or GL, reduced saturated fat and reduced energy are likely to be most effective, and these attributes are found in alternative sugars and sweeteners.

Further, experimental evidence shows that even in foods where saturated fat cannot easily be lowered, the use of alternative sweeteners in place of higher glycaemic sugars

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and dextrins will elicit a diminished glycaemic and insulin response. Enhancement of the latter by dietary fat is hardly possible with very-low-glycaemic sugars and sweeteners, thus reducing a possibility of atherogenic insulinaemia. In such products, a reduced glycaemic and insulinaemic response owing to the use of low-glycaemic carbohydrates is a valuable objective, while use of additional saturated fats to reduce the acute-glycaemic response should be avoided.

Lastly, the potentiation of hyperglycaemia-induced overproduction of superoxides from the mitochondrial respiratory chain provides a possible mechanism of oxidative damage, aging, tumour formation, atherogenic endothelial damage and of diabetic complications.¹¹⁰ Low-glycaemic carbohydrates may be especially valuable in avoiding these conditions, especially because some damage appears irreversible with contribution to a phenomenon of 'hyperglycaemic memory' in which some progressive damage occurs despite normalisation of glycaemic control. Health maintenance rather than therapeutic measures to restore health may thus prove to be the better option.

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