The Need for Special Foods and Sugar Substitutes by Individuals with Diabetes Mellitus

JOHN M. TALBOT AND KENNETH D. FISHER

The need for special dietary products marketed for use by individuals with diabetes mellitus and the safety and efficacy of certain nutritive sweetener substitutes for sucrose are reviewed. Special foods for individuals with diabetes mellitus are not necessary to achieve the dietary objectives recommended by leading United States and European authorities. They can be achieved conveniently and at minimum expense through enlightened choices of commonly available food items. At present, specific and unique characteristics of food products with special therapeutic properties for diets of diabetic individuals cannot be delineated or defined on rational nutritional grounds. Such terms as "diet," "dietetic," and "diabetic" on food labels have no uniform meaning for consumers, and diabetologists have observed that patients tend to consume such foods without regard to their energy content. Some consumers regard the reduced-calorie and low-calorie prepared food products as convenient in diets for weight reduction and diabetes although their use in dietary management of diabetes has no therapeutic basis other than weight reduction and maintenance. When fed as pure substances to fasted subjects, the nonglucose carbohydrate nutritive sweeteners, fructose, xylitol, and sorbitol, are absorbed relatively slowly and produce less postprandial hyperglycemia and insulin response than sucrose or glucose. Adequate studies of their long-term effectiveness when ingested as part of mixed meals have not been conducted. Although these sucrose substitutes are generally considered safe, the significance of recent information on possible carcinogenicity of oral xylitol in long-term feeding studies has not been fully evaluated. In view of the lack of certain essential information on the long-term effectiveness of various diets in preventing or mitigating the chronic debilitating complications of diabetes, suggestions for future research are included. DIABETES CARE 1: 231–240, JULY–AUGUST 1978.

There are a number of questions related to the possible need for special foods and sucrose substitutes by individuals with diabetes mellitus. Because these questions are of concern to the Food and Drug Administration (FDA), the Bureau of Foods, FDA, requested that the Life Sciences Research Office, Federation of American Societies for Experimental Biology (FASEB), undertake a study to review available scientific information, obtain the opinions of diabetologists, laboratory investigators, and epidemiologists, and prepare a comprehensive report on these issues. To assist in this review, an ad hoc study group of special consultants met at FASEB headquarters on July 18, 1977. (Study group members are listed at the end of this article.)

The resulting report (available from the Life Sciences Research Office, FASEB, 9650 Rockville Pike, Bethesda, Md. 20014) entitled, “The Need for Special Foods and Sugar Substitutes by Individuals with Diabetes Mellitus,” presents a synopsis of current information on diabetes mellitus and a brief review of FDA regulatory proposals on certain foods for special dietary purposes. It explores the dietary management of diabetes, emphasizing currently recommended principles and the use of nutritive nonglucose carbohydrate sweeteners in diabetic diets. However, nonnutritive synthetic sweeteners such as saccharin and cyclamate are not considered in the report. The question of the need for special foods, including foods marketed as “dietetic” and “diabetic” is addressed. The deliberations of the ad hoc group and a review of the scientific
literature provided the basis for the topics treated in the report.

BACKGROUND INFORMATION

It is estimated that in the United States there are about 4.2 million persons with diagnosed diabetes and roughly 5.5 million more with undiagnosed diabetes. The true prevalence of diagnosed diabetes in this country is uncertain, but a crude estimate is 2 per cent of the population. The prevalence appears to be increasing at a rate of about 6 per cent per year, and it is predicted that this trend will continue unless a cure or prevention can be found. According to West, 70 to 90 per cent of diabetic individuals in most affluent Western societies "are of the far, adult-onset type, while about 5 to 10 per cent are lean, youth-onset cases with little or no endogenous insulin and severe diabetes." There are several other less common types. Many patients have normal life spans, but, on the average, life expectancy is reduced by about one third in adult-onset diabetes and by somewhat more in juvenile-onset cases. Morbidity rates from vascular disease are decidedly excessive in diabetes.

West summed up the treatment of diabetic patients in this country: "In the United States about one-quarter of the known diabetics are being treated with insulin, about half are receiving oral agents, and about one-quarter are not receiving any antidiabetic medication." He indicated that the high rate of medicinal therapy reflects primarily the low frequency of successful use of available, effective long-term diet therapy.

Except when otherwise noted, in this report the term juvenile-onset diabetes refers to symptomatic, insulin-dependent, ketosis-prone, unstable, overt diabetes, and maturity-onset or adult-onset pertains to the mild to moderately severe, ketosis-resistant, overt diabetes as well as to the chemical or asymptomatic type.

FOODS MARKETED FOR USE IN DIABETES AND WEIGHT CONTROL

Sugar (Sucrose) Substitutes
Food products that are presently available in American markets in which substitutes for sucrose such as fructose, sorbitol, xylitol, and mannitol are used include chewing gums, candies, cookies, and cake mixes. Similar products are readily available in certain western European countries such as Germany, Switzerland, and Finland. Jams, jellies, and compotes containing these nutritive sweeteners are also available in Europe. In the United States, the Code of Federal Regulations defines the authorized uses as food ingredients of sorbitol [21 CFR 184.1835], mannitol [21 CFR 180.25 and 182.5470], and xylitol [21 CFR 172.395].

Other Dietary Products Represented as Useful in Weight Control and/or Diabetes
In the United States there are several hundred food products whose label statements indicate that they contain no or few calories or decreased levels of sugars, carbohydrates, or fats. The labels also claim that the products are "diet," "dietetic," "diabetic," "for diabetics," or "for diabetes" and/or are artificially sweetened. These products range from non-alcoholic beverages through food categories including baked goods, grain products, milk products, cheese, confections, preserves, fruits, salad dressings, meat products, soups, and snack foods. While most contain nonnutritive sweeteners such as saccharin, some contain nutritive sugar substitutes such as fructose, sorbitol, xylitol, or mannitol.

Confusion prevails about the meanings of such terms as "dietetic" and "diabetic" when they are applied to foods and food labels. A recent FDA survey revealed that 22 per cent of respondents understood the word "dietetic" on a food label to mean for use in a weight-reducing diet and 28 per cent understood the term to mean for use by persons with diabetes. The balance of the responses was divided among 10 other answers. Similarly, 36 per cent thought "diet" foods were for weight reduction and 9 per cent thought they were for diabetic patients with the balance of the answers divided among 10 unrelated answers.

A recently published tentative order on label statements restricts the use of the terms "diet" and "dietetic" in or in relation to label statements on products identified for use by diabetic patients. In the order announced on July 19, 1977, FDA proposed revised label statements for special dietary foods for use in reducing or maintaining body weight or caloric intake or in the diet of individuals with diabetes mellitus. The order, which has a tentative effective date of July 1, 1979, would prevent misleading label statements on foods that are not useful for these purposes and improve labeling in terms of meaningful content and legibility.

DIETARY MANAGEMENT OF DIABETES MELLITUS

From about 1950 to 1970 most American physicians adhered to the high-fat, restricted-carbohydrate concept that, coupled with weight reduction and maintenance of ideal body weight, formed the basic tenets of dietary management in diabetes. After evaluating all available scientific evidence, the American Diabetes Association issued in 1971 a landmark revision of dietary principles in a report by its Committee on Food and Nutrition.

Bierman and Nelson reviewed the scientific rationale for these newly enunciated principles, which were based on recognition that: (a) the only method of producing a remission with reasonable consistency is via weight reduction and adherence to ideal body weight; (b) the reduced glucose tolerance of diabetes is frequently normalized by weight reduction alone; (c) high-carbohydrate diets do not result in hyperglycemia and glucosuria in most diabetics provided that caloric intake is appropriate; and (d) there are significant advantages in allowing diabetic patients a normal proportion
of carbohydrates. In practical terms, these principles were the basis of a recommendation for restriction of total calories to achieve ideal body weight and a low-fat diet in which calories from fat are reduced and replaced by carbohydrate (starch, not sugar). Most patients can consume 45 to 60 per cent of total calories as carbohydrate. The long-standing advice to restrict intake of simple sugars was retained. Among the reasons for this was the mitigation of postprandial hyperglycemia.

These dietary recommendations have been advocated on the basis of available scientific evidence and clinical judgment without benefit of long-term prospective studies in human patients; however, as reviewed by West, they are supported by a number of clinical, laboratory, and epidemiological investigations. Whether or not dietary treatment, coupled as may be needed with antidiabetic medication, will aid in preventing and/or ameliorating atherosclerosis and the serious degenerative concomitants of diabetes remains to be established. Not all diabetologists agree with the consensus expressed above. Some still attach priority to restriction of total carbohydrate even in patients whose levels of caloric intake are optimal.

**Current Concepts and Principles**

The special report of the American Diabetes Association Committee on Food and Nutrition is widely acknowledged as a consensus representing the current thinking of most of America's leading diabetologists. The American Diabetes Association and the American Dietetic Association recommend: (a) restriction of total caloric intake to achieve and maintain ideal body weight while simultaneously providing adequate nutrition; (b) allowance of 45 to 60 per cent of total calories as carbohydrate, with a corresponding reduction in calories from saturated fats; and (c) prevention of hyperglycemic peaking and hypoglycemic dipping by proper scheduling and regularity of eating; avoidance of fasting, feasting, and simple, rapidly absorbed sugars; and by regular exercise. Avoidance of fasting is particularly important in juvenile-onset type of diabetes because of a risk of hypoglycemic brain damage.

As aids to patients, physicians, dietitians, and nurses in planning diets, the American Diabetes Association and the American Dietetic Association jointly published Exchange Lists for Meal Planning and A Guide for Professionals: The Effective Application of "Exchange Lists for Meal Planning".

**Other Dietary Concepts and Principles**

Weight reduction and maintenance of ideal body weight in the obese, maturity-onset diabetic patient are considered essential because these measures alone have the potential of controlling and even reversing the disease. West, while acknowledging the general lack of success in treating obesity, emphasizes that the benefits of weight reduction in overweight patients justify substantial therapeutic efforts in dietary management.

The ad hoc study group reiterated these principles and objectives and used them as a basis for discussion. Some consultants considered that control of saturated fat intake may be as important as calorie control in preventing or ameliorating the vascular complications of diabetes. However, it was pointed out that not all physicians who treat diabetic patients would agree with the recommended liberalization of carbohydrate calories and the corresponding reduction of fat. Based on the empirical finding that hyperglycemia and glucosuria appear to be more readily controlled with a diet in which carbohydrate is limited to about 50 to 70 per cent of the usual carbohydrate intake, some physicians prefer the long-standing dietary principle in which calories from carbohydrate are restricted and replaced by calories from fat.

The widely held notion that sucrose has no place in the diet of individuals with diabetes is not supported by scientific data. However, because simple sugars, particularly glucose and sucrose, are rapidly absorbed and can produce hyperglycemic peaks, their use by diabetic patients should probably be avoided because of the possibility that repeated exposure to hyperglycemia may damage blood vessels and nerves. However, sucrose may be appropriate to prevent hypoglycemia in diabetic individuals before or during heavy exercise. Some experts believe that in the large group of maturity-onset diabetic patients, who, under clinical treatment, do not show much glucosuria over the 24-hour period but may have some hyperglycemia, the consumption of sucrose in modest amounts may be harmless when it is a part of their restricted calorie diet. Consumption of high sucrose foods between meals as snacks, such as soft drinks or a glazed doughnut, is considered undesirable by many diabetologists; but it is noteworthy that fresh fruits and fruit juices are commonly prescribed in diabetic diets. These usually contain substantial amounts of readily available glucose, invert sugar, or sucrose.

A major problem in promulgating dietary guidelines to professionals and patients is that the dietary objectives differ greatly in the two main types of diabetes. In cases of juvenile-onset type diabetes or in pregnant women with diabetes, the diet must provide sufficient total calories to meet the growth and development requirements. Unlike most individuals with maturity-onset diabetes, who tend toward obesity, those with juvenile-onset diabetes are typically underweight, and dietary restrictions must be carefully balanced with provision of sufficient calories and essential nutrients. For patients with juvenile-onset diabetes who are receiving insulin, three main meals and a daily bedtime snack are recommended, with the added suggestion that a midmorning and/or a midafternoon snack may be useful. Between-meal intervals should not exceed five hours except at night.

**Nonglucose Carbohydrates as Sucrose Substitutes**

To improve the acceptability and attractiveness of foods for individuals who prefer sweet items with their meals or snacks, investigators have long searched for sugar substitutes that would be com-
patible with diets for diabetic patients. Certain advantages of using fructose, sorbitol, or xylitol as substitutes for sucrose in diabetic diets have been reported by European investigators, and, for example, it is common practice in West Germany to use fructose or xylitol in diabetic diets. This is based on recognition of the importance of the need for sweetness and the concept that sweeteners that cause the least disturbance of carbohydrate metabolism should be used. Satisfying the human craving for sweetness is considered by some authorities as an important aspect of the process of acquiring good patient compliance with the diabetic diet prescription. For example, of 500 diabetic patients questioned by Mehnert, only 84 expressed willingness to do without sweet-tasting foods. Fifty-seven regularly used sorbitol, eight used fructose, and 351 used either cyclamate or saccharin. (At the time of that study, xylitol was not generally available.)

Some nutritive carbohydrates that have been recommended as sugar substitutes for use by diabetic patients are fructose, sorbitol, and xylitol. These have been called non-glucose carbohydrates and are extensively used in diabetic diets in some western European countries, particularly West Germany and Switzerland.

**ABSORPTION AND METABOLISM**

These nonglucose carbohydrates are absorbed from the alimentary canal more slowly and to a lesser degree than the ordinary dietary sugars. Compared with sucrose, glucose and maltose, their use leads to less postprandial hyperglycemic peaking, a result in part of slower absorption; the hyperglycemia that does occur with these nutrients is slower in onset and of less magnitude, reducing the need for endogenous insulin in the postprandial period. Aside from a dose-related osmotic diarrhea from excessive amounts of sorbitol and, to a lesser extent, of xylitol, these substances are generally regarded as harmless when used as foods or food ingredients.

Unlike glucose, most of their initial metabolism occurs in the liver independently of insulin; however, because they are partly converted to glucose, their metabolism is not entirely insulin independent. Nevertheless, in relation to the derangements of glucose metabolism in diabetes, less insulin is needed in a given period of time to keep the blood glucose concentration constant when some sucrose or glucose is replaced by fructose, sorbitol, or xylitol. Their partial conversion to glucose proceeds at a relatively slow rate governed primarily by their rate of absorption and the metabolic mode of the liver, gluconeogenic with low insulin and high glucagon or glycolytic with high insulin and low glucagon; however, the degree of long-term reduction of the insulin requirement has not been well demonstrated.

According to Cook, 80 to 90 per cent of ingested fructose is absorbed in the human jejunum as fructose and is then rapidly taken up by the liver. In the liver it undergoes transformation to fructose-1-phosphate and then to dihydroxyacetone phosphate and free glyceroldehyde. Glyceroldehyde is subsequently phosphorylated to glyceroldehyde phosphate. The dihydroxyacetone phosphate and glyceroldehyde phosphate may then undergo glycolysis or transformation to fructose-6-phosphate and ultimately to glucose. Even when large doses of fructose are administered intravenously to human subjects, the available evidence indicates a conversion of about one third to circulating glucose, suggesting that fructose metabolism is largely by the liver. In diabetic patients receiving as much as 450 gm. of fructose daily by continuous gastric intubation, no significant amount of fructose is detectable in the arterial blood. Sorbitol and xylitol are also metabolized preferentially in the liver, sorbitol via transformation to fructose and xylitol via D-xylulose-5-phosphate to glyceroldehyde phosphate and fructose-6-phosphate. Fructose-6-phosphate is convertible to glucose and glycogen, and glyceroldehyde phosphate to glucose, glycogen, and via the glycolytic pathway, to lactic acid.

Animal experiments have shown that substantial amounts of fructose, sorbitol, and xylitol are rapidly converted to glucose by the liver via the insulin-independent metabolic pathways outlined above and that the utilization of this glucose in such tissues as liver, muscle, and fat is clearly insulin dependent. Nevertheless, these sugar substitutes do not produce significant hyperglycemia in normal (nondiabetic) animals and man in the postabsorptive state.

**POTENTIAL ADVANTAGES**

The theoretical and practical advantages of using fructose, sorbitol, and xylitol in diabetic diets have been reviewed by Dehmel et al., Cook, Cook; Lang; Brin and Miller; Mehnert and Förster; Scheinin and Mäkinen; Touster; Dwivedi; and Turner et al.

These investigators have reported the following general conclusions: (a) Fructose, sorbitol, and xylitol are generally considered safe when taken orally. (b) Their ingestion does not result in significant postprandial hyperglycemia or in the hyperglycemic peaking that follows ingestion of the rapidly absorbed simple sugars such as glucose and sucrose. (c) Less insulin is needed to keep the blood glucose constant in the postprandial period. (d) They are absorbed from the bowel more slowly than sucrose, glucose, and maltose, and are rapidly taken up by the liver in the absence of insulin. (e) They are metabolized principally in the liver, partially independently of insulin; they enter the metabolic pathway of glucose by different routes and at different steps. (f) Their metabolic conversion to glucose in the liver proceeds at a steady rate mainly determined by their relatively slow absorption and the nature of the sequence of hepatic metabolic reactions. (g) Fructose, sorbitol, and xylitol tend to decrease
keto genesis. (h) Contrary to data from previous studies, recent investigations indicate that, compared with glucose, fructose even in large amounts does not increase blood triglycerides in humans. (i) Animal data indicate that some fructose is taken up by fatty tissues in the absence of insulin. (j) Patients who use these sugar substitutes tend to follow their diabetic diet prescriptions more faithfully than those whose physicians deny them access to such substances. (k) In fasting experimental animals, these substances exert a direct nitrogen-sparing effect that is not dependent on glucose metabolism and insulin secretion. (l) They are superior to the nonnutritive artificial sweeteners for sweetening certain foods because they behave like sucrose during food preparation, requiring no additives for viscosity and bulking, and they do not leave an unpleasant aftertaste. (m) Except for sorbitol, they compare favorably with sucrose in sweetness, and under most conditions fructose confers more sweetness per calorie. (n) Xylitol appears to have noncariogenic properties that may be of great value, and sorbitol has been shown to be substantially less cariogenic than sucrose.

In contrast to the experimental and clinical data that suggest the nonglucose carbohydrate sweeteners offer advantages in the dietary treatment of diabetes, Arvidsson-Lenner reported no significant differences in postprandial blood glucose levels and glucosuria when isocaloric test meals containing sucrose, fructose, or sorbitol were fed to nine human adult diabetic and three healthy adult subjects.

POSSIBLE DISADVANTAGES

The relatively slow absorption of fructose, sorbitol, and xylitol from the intestine may result in osmotic diarrhea and flatulence when subjects ingest excessive amounts in single doses; for instance, single, diarrheagenic oral doses in humans have been reported as 70 to 100 gm. fructose, 20 to 30 gm. sorbitol, and 30 to 40 gm. xylitol. However, large individual differences exist in tolerance to these substances. Sustained use of xylitol leads to adaptation so that higher doses become tolerable. The practical amounts of these substances needed for use as sugar substitutes are generally below the laxation levels.

Well-known side effects of high doses of most carbohydrates include increased serum uric acid, bilirubin, and lactate, with a tendency toward acidosis. Fructose and the sugar alcohols produce several of these effects such as increased serum lactate levels and lactate-pyruvate ratios and decreased concentrations of free fatty acids and phosphate. In addition, oral administration of fructose, sorbitol, and xylitol, as well as sucrose, increases serum uric acid concentration. In a more recent report, Förster concluded that, except for the increase in uric acid synthesis, these sugar substitutes cause no specific and dramatic side effects. However, in long-term studies with normal human subjects who ingested fructose or xylitol as part of the diet, serum levels of triglycerides, glucose, insulin, urate, lactate, and pyruvate did not differ significantly from those of subjects who consumed sucrose as part of the diet. Rapid intravenous administration of fructose, xylitol, or sorbitol at high doses may result in increased uric acid production, a transient decrease of hepatic inorganic phosphate, and, mainly with fructose, increased lactate production. However, no significant side effects occur after oral administration of fructose, xylitol, or sorbitol at levels that are isocaloric with average amounts of sucrose added to foods.

Thomas et al. reported adverse reactions to intravenous administration of solutions containing xylitol in 10 of 22 patients. In response to solutions of up to 50 per cent xylitol in distilled water, individual patients exhibited one or more of the following: diuresis, lactic acidosis, hyperuricemia, crystal deposits of calcium oxalate in the renal tubules with tubular epithelial damage, oliguria, azotemia, and cerebral and hepatic disturbances. As a result, parenteral and oral use of xylitol was banned in Australia. It is noteworthy that the patients in these studies were all suffering from severe illnesses that may have compromised crucial physiologic functions such as renal excretion. Froesch and Jakob emphasized the danger of lactic acidosis if large amounts of fructose, sorbitol, or xylitol are administered parenterally.

Of the adverse reactions reported by the Australian investigators, the question of parenteral xylitol as a causal factor in the induction of oxalosis and deposition of calcium oxalate crystals appears one of the most pressing. In a recent review of the effects of using nonglucose carbohydrates parenterally, Ahnfeldt and associates concluded that observation of proper dosage guidelines avoids the possible side effects that have been described including deposition of oxalate crystals.

Hauschmidt and her associates conducted clinical investigations to determine whether xylitol infusions are associated with biochemical reactions that promote calcium oxalate crystallization. Although none of the patients showed hyperoxaluria or hyperuricemia after xylitol infusions, glycolate excretion increased by two or three orders of magnitude together with an increased excretion of tetronic acids. The authors suggested that while xylitol breakdown may generate oxalate precursors, oxalosis occurring in association with xylitol infusions is caused by some factor other than the metabolism of xylitol and that the most likely predisposing variable involved in the reported Australian cases were abnormal renal function. Finally, Wang et al. considered it highly unlikely that oxalate formation was the cause of the toxicity in the cases reported from Australia by Thomas et al.

The possible influence of sorbitol and xylitol on cataract formation was discussed at the ad hoc group meeting, and the consensus was that exogenous sorbitol and xylitol have no specific or direct influence on cataractogenesis.

Consideration of the advantages and disadvantages of...
fructose, sorbitol, and xylitol used as substitutes for glucose, sucrose, and maltose, suggests that no obvious toxic effects result from their oral and parenteral use provided that intravenous use does not exceed 0.25 gm. per kilogram per hour and oral intake is approximately isocaloric with average amounts of sucrose added to foods. For diabetic patients, their contribution to total caloric intake must be duly recognized. Fructose and xylitol may offer some advantage, albeit slight, over sucrose or glucose in diabetic diets. Because of its somewhat pronounced diarrheagenic characteristic and its relatively low sweetness, sorbitol was thought to provide little advantage to the patient in the dietary management of diabetes mellitus.

However, feeding trials conducted at the Huntingdon Research Centre, England, suggest that xylitol in the diet is associated with tumor induction in experimental animals. Preliminary data from these studies indicate that mice fed xylitol at levels of 2, 10, and 20 per cent of the diet for two years have increased urinary bladder calculi and an associated dose-related bladder epithelial hyperplasia and neoplasia in males receiving xylitol at the 10 and 20 per cent levels. Similar chronic xylitol feeding studies in rats and dogs at the same laboratory did not show the changes reported in the mice. However, male rats given 20 per cent xylitol in the diet showed an increased incidence of adrenal medullary neoplasms. Final conclusions from these investigations await completion of data analysis, and expanded studies have only recently been initiated. In this connection, it should be noted that Batzinger et al. have shown that xylitol exhibited no mutagenic activity in microbial assay and host-mediated assay test systems. Using a modified Ames test system with Salmonella typhimurium strains TA 100 and TA 98, these investigators found no mutagenic activity when xylitol was tested directly, in urine of mice fed xylitol both with and without liver microsomal fractions (S9) or in results of the host-mediated assay.

Concern for mutagenicity and carcinogenicity of xylitol requires that additional studies be undertaken to clarify the results reported in these two investigations.

EVOLVING CONCEPTS AND TRENDS

Additional support for the American Diabetes Association and The American Dietetic Association recommendations should accumulate as more clinical experience is reported on improved glucose tolerance and metabolic status of diabetic patients who receive careful dietary management.

Some experts believe that restriction of saturated fat intake may be as important as control of total caloric intake in terms of atherogenesis. In addition, the role of certain environmental factors is unclear; for example, the effect of low-molecular weight compounds in the diet, such as inositol, on diabetic neuropathy.

The question of liberalizing the use of sucrose or sucrose-containing foods continues to be of concern. Isocaloric substitution of small amounts of natural or refined sucrose for other nutrients usually has little effect on levels of glycosuria or hyperglycemia. Nevertheless, in poorly controlled diabetic patients, refined sucrose is not advisable, mainly because, when used as part of major meals, sugars tend to produce sharp elevations of blood glucose. Recently published data suggest the possibility of improving the selection of complex carbohydrates in the diet to minimize postprandial hyperglycemia and insulin response.

Economic, biologic, and educational factors will influence the future use of the nutritive nonglucose carbohydrates. The industrial use of high-fructose corn syrup (approximately 42 per cent fructose, 52 per cent glucose) as a substitute for sucrose amounted to about 6 per cent of the total sweetener market in 1975. However, a trend toward increased use of fructose is anticipated. Estimates of probable increasing use of high fructose corn syrup during the next 10 to 15 years vary from 14 to 30 per cent.

Certain manufacturers of xylitol and of foods in which sucrose is replaced by one or more of the nonglucose carbohydrates are marketing their products in this country at the present time or are preparing to do so. Two important findings that may stimulate the use of these substances are the noncarcinogenic properties of xylitol and the technical advantages outlined above of the nonglucose carbohydrates compared with other nutritive sweeteners when used in the diabetic diet. A biologic factor of fundamental importance concerns the unsettled question of whether precise maintenance of normoglycemia in diabetes exerts any favorable effect on the course of the disease. If future experience can document that it does, then the sugar substitutes may assume a firmer position as part of the diet provided that the issue of possible carcinogenicity of xylitol is resolved.

The fact that there is currently no generally acceptable artificial sweetener in the United States adds to the potential interest in these nonglucose carbohydrates. Because the non-glucose carbohydrates may offer some limited advantages when used as sugar substitutes in the dietary treatment of diabetes, interest in their use may be expected to increase.

SPECIAL FOODS IN THE DIETARY MANAGEMENT OF DIABETES

In addition to the role of nutritive nonglucose carbohydrate sweeteners, the possible efficacy of and need for specially formulated foods in the dietary management of diabetes were central issues in this review. Consequently, considerable discussion was devoted to the so-called "dietetic" and "diabetic" foods and to a judgment as to whether foods for special dietary use intended specifically for diabetic patients can be identified and defined.

On the basis of current information, it is unlikely that
foods for special dietary use intended specifically for persons with diabetes mellitus can be delineated or defined on rational nutritional grounds. Few authorities support the notion that such special foods are necessary. In fact, with the possible exceptions of water-packed fruits and the artificially sweetened soft drinks, labels indicating usefulness in dietary management of diabetes are often undesirable and frequently misleading because patients may be led to believe that they may consume such foods freely without adding calories to their daily caloric allowance. Furthermore, the use of “dietetic foods” complicates the problem of estimating total caloric intakes and of dividing the diet into proper proportions of carbohydrates, proteins, and fats, particularly for patients who use exchange lists.

The only rational support for the use of “dietetic foods” by diabetic persons is as convenient aids to weight reduction and control; however, such specially formulated foods are not necessary to restrict caloric intake or in the dietary management of diabetes per se. These opinions of the consultants are consistent with those expressed in the publications of diabetologists, nutritionists, and others. 2,4,9,13,63,64

Specially formulated convenience or snack foods considered useful in the diet of diabetic individuals, in addition to the water-packed fruits, are artificially sweetened soft drinks such as the “diet colas.” In some western European countries, the jams, jellies, compotes, and bakery products sweetened with fructose, sorbitol, or xylitol are considered useful, but they are less widely recommended in the United States. Some diabetologists believe there is probably a need for an alternative to high-sweetness drinks, that is, a low-calorie, low-sweetness drink containing regular sweeteners. However, it is not known if this alternative would be technologically feasible or would prove generally acceptable among diabetic patients.

A majority of consultants in this study concluded that there is little value in the use of the terms “dietetic” and “diabetic” on labels of foods intended for use by persons with diabetes mellitus; however, they favor retention of the term “foods for special dietary use.” Food labels should be factual; for example, “water-packed, no sugar added.”

**SUMMARY AND CONCLUSIONS**

Leading authorities on the dietary management of diabetes mellitus affirm that the main emphasis in obese patients should be on control of caloric intake to achieve and maintain ideal body weight. Most authorities now recommend that dietary fat and sugar be reduced and that the proportion of calories as starch be increased in both of the main types of diabetes (obese, insulin independent and lean, insulin dependent). In addition, they believe there is a need for only a very few special foods for diabetic patients, specifically the water-packed fruits and the artificially sweetened, low-calorie soft drinks. Some diabetologists believe there may be a need for a selection of foods sweetened with the nonglucose carbohydrates; for instance if nonnutritive sweeteners such as saccharin are not available, then soft drinks containing a nonglucose carbohydrate sweetener might be as useful as the artificially sweetened soft drinks in terms of palatability and acceptability provided that their long-term influence on blood sugar levels was innocuous.

The principal conclusions of this study are:

- There are insufficient data to determine if sorbitol, xylitol, or other polyols substituted for conventional sweeteners such as sucrose, or when indigenous to food, have special nutritional or other significance in the long-term dietary management of diabetes. When fed as pure substances to fasted subjects, these nonglucose carbohydrate nutritive sweeteners are absorbed relatively slowly and produce less postprandial hyperglycemia and insulin response than sucrose or glucose. However, adequate studies of their long-term effectiveness
when ingested as a part of mixed meals have not been conducted.

—There are insufficient data to determine if fructose or any other carbohydrate has beneficial properties for the long-term dietary management of diabetes. When fed as a pure substance to fasted subjects, fructose is absorbed fairly slowly and postprandial hyperglycemia and insulin response are less than those with sucrose or glucose. However, adequate studies of the long-term effectiveness of fructose ingested as a part of mixed meals have not been conducted.

—Despite these deficiencies in knowledge, the ad hoc review group acknowledged that the use of sorbitol, xylitol, or fructose is accepted by reputable European diabetologists and that these substitutes may provide some minor advantages in dietary management of diabetes mellitus.

—The evidence that other foods or food ingredients may have beneficial properties in the dietary management of diabetes mellitus is limited. Special foods for diabetic individuals are not necessary to achieve objectives of dietary management and dietary principles recommended by leading United States and European authorities. These recommendations and dietary principles can be followed conveniently at minimum expense through enlightened choices of commonly available food items.

—There is no evidence suggesting value of dietetic foods in the dietary management of diabetes other than their usefulness in weight reduction or weight control.

—Specific and unique characteristics of food products with special therapeutic properties for diets of diabetic individuals cannot currently be delineated or defined on rational nutritional grounds.

Suggestions for Future Investigation

More data are needed on the metabolic effects of substitute nutritive sweeteners such as fructose, xylitol, and sorbitol in foods as they are consumed in regular diets. For instance, prospective studies are needed on 24-hour and 30-day effects on blood sugar, insulin response, and other parameters as a result of administering varying amounts of fructose, sucrose, sorbitol, and xylitol in different combinations in the diets of (1) persons with mild cases of adult-onset diabetes where fasting blood sugars are normal but glucose tolerance tests are abnormal; (2) mild or moderately severe maturity-onset diabetes patients with persistent fasting hyperglycemia; and (3) lean, juvenile-onset, insulin-dependent diabetic individuals. The effects of controlling blood glucose during the 24-hour period as well as from minute-to-minute are not well defined. The results of such studies would suggest other important avenues of research.

More clinical and metabolic data are needed on the effects of foods sweetened with fructose and other sucrose substitutes used as parts of the main meals versus between meal snacks and drinks in the acute management of patients with insulin-dependent diabetes.

Certain studies of the effects on blood glucose levels and urinary glucose losses of substituting fructose or sorbitol for sucrose in prescribed diabetic breakfast meals suggest that fructose or sorbitol has little, if any, advantage over sucrose in well-regulated patients with maturity-onset diabetes mellitus. It appears unnecessary to have specially sweetened foods designed for adult individuals with this type of diabetes. The differences between these results and other studies showing metabolic advantages for fructose, sorbitol, or xylitol in the dietary management of diabetes should be resolved using both insulin-dependent and insulin-independent diabetic subjects.

More animal and prospective clinical and epidemiological studies are needed to determine what elements of the diet are crucial in terms of the debilitating concomitants of diabetes; for example, neuropathy, retinopathy, and coronary artery disease.

Additional investigation of fructose metabolism in normal and diabetic animals and human subjects is needed. Examples of pertinent questions include the effects on blood lipids when substantial amounts of fructose such as 100 to 150 gm. per day are consumed; the long-term effects of reducing sucrose intake by 50 per cent and replacing this with fructose; whether or not the cariogenic bacteria may become fructose rather than glucose dependent; the long-term effects on glycoproteins; and whether or not toxic metabolites may result from the more rapid formation of Schiff-bases with fructose compared with glucose.

Additional studies are required on the effects of fructose, xylitol, and sorbitol on glycoproteins in relation to atherosclerosis, particularly in human subjects.

The possible carcinogeticity of orally administered xylitol requires concerted attention if this nutritive noncaloric sweetener is to have a greater role in dietary management of diabetes mellitus.

The effects of fructose, sorbitol, and xylitol on weight reduction and weight maintenance in obese diabetic patients should be investigated. In addition, their ability to support weight gain in the juvenile-onset diabetic patient requires investigation.

More comparative data are desirable on the relative sweetness of products prepared with fructose as they might be consumed in typical American diets.

There is insufficient scientific information on the influence of dietary fiber on the absorption and metabolism of carbohydrates to determine its possible beneficial or adverse effects. The absence of hyperglycemia that has been reported in subjects taking certain types of dietary fiber with their diets may be a result of interference with carbohydrate absorption. The influence of the level and type of dietary fiber on carbohydrate absorption needs clarification.

Uncertainties about the long-term effects of large amounts of unsaturated fats in the diet on the course of diabetes mellitus require further investigation.
Additional investigations are advisable on the influence of certain environmental factors on the prevention and amelioration of diabetes complications, for example, small molecular weight compounds such as inositol in relation to neuropathy.

Although difficult to obtain, more information is needed on the comparative risks of disturbed carbohydrate metabolism and development of complications in diabetic patients who consume refined sugar versus those who avoid it, and how much refined sugar is allowable, particularly for persons with insulin-dependent diabetes. Similarly, there are unanswered questions about the advisability of a liberal carbohydrate diet for individuals with moderately to poorly controlled diabetes.

ACKNOWLEDGMENT: This study was supported by Contract Number FDA 223-75-2090, Food and Drug Administration, Department of Health, Education and Welfare.

The group of consultants included R. A. Arky, M.D., Cambridge, Mass.; K. H. Bässler, M.D., Mainz, W. Germany; E. L. Bierman, M.D., Seattle; J. D. Brunzell, M.D., Seattle; G. F. Cahill, Jr., M.D., Boston; W. H. Daughaday, M.D., St. Louis; J. K. Davidson, III, M.D., Ph.D., Atlanta; A. D. Morrison, M.D., Philadelphia; O. Touster, Ph.D., Philadelphia; and K. M. West, M.D., Oklahoma City. Food and Drug Administration participants were J. Chopra, M.D., V. P. Frattali, Ph.D., and J. E. Vanderveen, Ph.D. Life Sciences Research Office participants were H. I. Chinn, Ph.D.; K. D. Fisher, Ph.D.; K. K. Kimura, Ph.D, M.D.; F. R. Senti, Ph.D.; and J. M. Talbot, M.D. T. E. Huber, M.D., Bethesda, Md., was a special consultant.

From the Life Sciences Research Office, Federation of American Societies for Experimental Biology, Bethesda, Maryland 20014.

Address reprint requests to J. M. Talbot, Life Sciences Research Office, FASEB, 9650 Rockville Pike, Bethesda, Md. 20014.

REFERENCES


240 DIABETES CARE, VOL. 1 NO. 4, JULY-AUGUST 1978