EVALUATION OF THE HEALTH ASPECTS OF
SUCROSE AS A FOOD INGREDIENT

1976

Prepared for

Bureau of Foods
Food and Drug Administration
Department of Health, Education, and Welfare
Washington, D.C.

Contract No. FDA 223-75-2004
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Life Sciences Research Office
Federation of American Societies
for Experimental Biology
9650 Rockville Pike
Bethesda, Maryland 20014
NOTICE

This report is one of a series concerning the health aspects of using the Generally Recognized as Safe (GRAS) or prior sanctioned food substances as food ingredients, being made by the Federation of American Societies for Experimental Biology (FASEB) under contract no. 223-75-2004 with the Food and Drug Administration (FDA), U.S. Department of Health, Education, and Welfare. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshalling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office (LSRO), established by FASEB in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

Qualified scientists were selected as consultants to review and evaluate the available information on each of the GRAS substances. These scientists, designated the Select Committee on GRAS Substances, were chosen for their experience and judgment with due consideration for balance and breadth in the appropriate professional disciplines. The Select Committee's evaluations are being made independently of FDA or any other group, governmental or nongovernmental. The Select Committee accepts responsibility for the content of each report. Members of the Select Committee who have contributed to this report are named in Section VII.

Tentative reports are made available to the public for review in the Office of the Hearing Clerk, Food and Drug Administration, after announcement in the Federal Register, and opportunity is provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the substances covered by the report. The data, information, and views presented at the hearing are considered by the Select Committee in reaching its final conclusions. Reports are approved by the Select Committee and the Director of LSRO, and subsequently reviewed and approved by the LSRO Advisory Committee (which consists of representatives of each constituent society of FASEB) under authority delegated by the Executive Committee of the Federation Board. Upon completion of these review procedures the reports are approved and transmitted to FDA by the Executive Director of FASEB.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of all of the individual members of its constituent societies.

C. Jelleff Carr, Ph.D., Director
Life Sciences Research Office
FASEB
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I. INTRODUCTION

This report concerns the health aspects of using sucrose as a food ingredient. It has been based partly on the information contained in two scientific literature reviews (monographs) furnished by FDA (1), which summarize the world's scientific literature from 1920 through 1974.* To assure completeness and currency as of the date of this report this information has been supplemented by searches of over 30 scientific and statistical reference sources and compendia that are generally available; use of new, relevant books and reviews and the literature citations contained in them; consideration of current literature citations obtained through computer retrieval systems of the National Library of Medicine; searches for relevant data in the files of FDA; and by the combined knowledge and experience of members of the Select Committee and the LSRO staff. In addition, announcement was made in the Federal Register on January 22, 1976 (41 FR 3332 to 3334) that opportunity would be provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the health aspects of using sucrose as a food ingredient. Four requests were received. The Select Committee held a hearing on May 24, 1976. Those who requested opportunity to present data, information, and views are identified at the end of this report. The material presented at the hearing has been considered by the Select Committee in reaching its final conclusions.

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321(s)], GRAS substances are exempt from the premarketing clearance that is required for food additives. It is stated in the Code of Federal Regulations 21 CFR 121.1, revised April 1, 1976, that GRAS means general recognition of safety by experts qualified by scientific training and experience to evaluate the safety of substances on the basis of scientific data derived from published literature. This section of the Code also indicates that expert judgment is to be based on the evaluation of results of credible toxicological testing or, for those substances used in food prior to January 1, 1958, on a reasoned judgment founded in experience with common food use, and is to take into account reasonably anticipated patterns of consumption, cumulative effects in the diet, and safety factors appropriate for the utilization of animal experimentation data. FDA recognizes further (21 CFR 121.3) that it is impossible to provide assurance that any substance is absolutely safe for human consumption.

The Select Committee on GRAS Substances of LSRO is making its evaluations of this substance in full recognition of the foregoing provisions.

*These documents (PB-228 548/4, PB-241 963/8) are available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
In reaching its conclusions on safety, the Select Committee, in accordance with FDA's guidelines, is relying primarily on the absence of substantive evidence of, or reasonable grounds to suspect, a significant risk to the public health. While the Select Committee realizes that a conclusion based on such reasoned judgment is expected even in instances where the available information is qualitatively or quantitatively limited, it recognizes that there can be instances where, in the judgment of the Select Committee, there are insufficient data upon which to base a conclusion. The Select Committee, aware that biological testing is dynamic, bases its conclusions on information now available; it cannot anticipate the results of experiments not yet conducted or those of tests that may be reconducted, using new technologies. These conclusions will need to be reviewed as new or better information becomes available.

In this context, the LSRO Select Committee on GRAS Substances has reviewed the available information on sucrose and submits its interpretation and assessment in this report, which is intended for the use of FDA in determining the future status of this substance under the Federal Food, Drug, and Cosmetic Act.

II. BACKGROUND INFORMATION

Sucrose, commonly known as table sugar, cane sugar, or beet sugar, is a disaccharide of glucose and fructose (β-D-fructofuranosyl-α-D-glucopyranoside). It is the most abundant carbohydrate in the sap of land plants. Commercial sucrose, produced almost exclusively from sugar cane or sugar beets, is one of few organic compounds available in vast quantities, high purity and relatively low cost. Estimated world production in 1972 was about 74 million metric tons (2).

Sucrose is used by the food and other edible products industries primarily for sweetening; less than 1 percent goes into non-food uses. Of the more than ten million tons marketed as food in the United States annually, 25 percent is sold to home and 5 percent to institutional users; the remainder is used by the baking, confectionery, ice cream, beverage and other food industries (3).

Standards of identity and purity for sucrose are given in the U.S. Pharmacopeia VIII for pharmaceutical uses (4). A food-grade sucrose is not described in the Food Chemicals Codex (5).

Sucrose is generally recognized as safe (GRAS) in the Code of Federal Regulations [21 CFR 121.101(a)] (6).

The domestic food consumption of cane and beet sucrose as indicated by disappearance statistics has changed little in recent years. Per capita disappearance was 100 pounds in 1925-1929, 97.6 pounds in 1960 and 102.5 pounds in 1970 (7). These figures include sucrose added
during food preparation in the home or restaurant or by the individual to the food he consumes, plus that added by the food industry in the processing of foods. The percentage contributed by processed foods has increased from about 30 percent 50 years ago to 70 percent today (3). Data taken from a survey of the food industry made by a subcommittee of the National Research Council (NRC) believed to represent about 60 percent of the food industry show that the amount of sucrose used by the industry in processed foods and beverages doubled between 1960 and 1970 (8).

However, more reliable data collected by the U.S. Department of Agriculture indicates 1971 use of sugar in processed foods and beverages increased only 30 percent over that used in 1957-1959. Use in beverages, largely soft drinks, about doubled over this period (3).

It is noteworthy that total carbohydrate consumption as estimated from disappearance data in the United States has generally declined while total sucrose consumption has changed relatively little since 1925-1929. As a result, the proportion of total carbohydrate provided by sucrose has increased from about 20 percent to about 33 percent over this period. Decrease in total carbohydrate consumption has been due largely to reduction in the consumption of cereals and flour (3).

The NRC report (8) provides information on the usual levels of sucrose addition in various categories of processed foods (Table I). Based on the information supplied by those manufacturers who reported adding sucrose to at least one food product in a food category, a weighted mean was calculated for the usual percentage addition to foods in that category. For a given category, the mean of the addition levels reported by a manufacturer was weighted by the ratio of pounds used by that manufacturer in all categories to the pounds (all categories) used by those manufacturers that reported use in the category. It is to be noted that the weighted means do not express the highest percentage of sucrose added by any manufacturer; they do not indicate which specific foods in a category contain sucrose; and they do not necessarily coincide with the levels used by any one industry in its products in the food categories listed.

III. CONSUMER EXPOSURE DATA

The NRC subcommittee also provided information on possible average daily intakes of sucrose by age groups (Table II) (8). Since food consumption data were not requested in the subcommittee survey, intake estimates were derived by utilizing Market Research Corporation data on mean frequency of eating foods by category, USDA data on mean portion size,
# TABLE I

Level of Addition of Sucrose to Foods by Food Category (8)

<table>
<thead>
<tr>
<th>Food category</th>
<th>Weighted mean percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baked goods, baking mixes</td>
<td>11.42</td>
</tr>
<tr>
<td>Breakfast cereals</td>
<td>26.71</td>
</tr>
<tr>
<td>Grain products such as pastas or rice dishes</td>
<td>1.43</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>3.43</td>
</tr>
<tr>
<td>Milk, milk products</td>
<td>17.94</td>
</tr>
<tr>
<td>Cheese</td>
<td>24.56</td>
</tr>
<tr>
<td>Frozen dairy desserts, mixes</td>
<td>9.31</td>
</tr>
<tr>
<td>Processed fruits, juices and drinks</td>
<td>12.58</td>
</tr>
<tr>
<td>Fruit ices, water ices</td>
<td>12.38</td>
</tr>
<tr>
<td>Meat products</td>
<td>2.87</td>
</tr>
<tr>
<td>Poultry products</td>
<td>1.50</td>
</tr>
<tr>
<td>Eggs, egg products</td>
<td>1.90</td>
</tr>
<tr>
<td>Fish products</td>
<td>3.42</td>
</tr>
<tr>
<td>Processed vegetables, juices</td>
<td>13.25</td>
</tr>
<tr>
<td>Condiments, relishes, salt substitutes</td>
<td>26.82</td>
</tr>
<tr>
<td>Soft candy</td>
<td>44.74</td>
</tr>
<tr>
<td>Sugar, confections</td>
<td>39.86</td>
</tr>
<tr>
<td>Jams, jellies, sweet spreads</td>
<td>32.72</td>
</tr>
<tr>
<td>Sweet sauces, toppings, syrups</td>
<td>30.96</td>
</tr>
<tr>
<td>Gelatins, puddings, fillings</td>
<td>19.11</td>
</tr>
<tr>
<td>Soups, soup mixes</td>
<td>0.20</td>
</tr>
<tr>
<td>Snack foods</td>
<td>5.21</td>
</tr>
<tr>
<td>Beverages, nonalcoholic</td>
<td>13.04</td>
</tr>
<tr>
<td>Beverages, alcoholic</td>
<td>10.27</td>
</tr>
<tr>
<td>Nuts, nut products</td>
<td>8.14</td>
</tr>
<tr>
<td>Gravies, sauces</td>
<td>5.66</td>
</tr>
<tr>
<td>Dairy products analogs</td>
<td>16.24</td>
</tr>
<tr>
<td>Hard candy</td>
<td>48.98</td>
</tr>
<tr>
<td>Chewing gum</td>
<td>42.30</td>
</tr>
<tr>
<td>Granulated sugar</td>
<td>97.92</td>
</tr>
<tr>
<td>Instant coffee and tea</td>
<td>12.60</td>
</tr>
<tr>
<td>Seasonings and flavors</td>
<td>10.81</td>
</tr>
<tr>
<td>Baby cereals</td>
<td>2.55</td>
</tr>
<tr>
<td>Baby formulas</td>
<td>4.76</td>
</tr>
<tr>
<td>Baby processed fruit</td>
<td>12.25</td>
</tr>
<tr>
<td>Baby meat products</td>
<td>0.44</td>
</tr>
<tr>
<td>Baby poultry products</td>
<td>0.58</td>
</tr>
<tr>
<td>Baby processed vegetables</td>
<td>2.89</td>
</tr>
<tr>
<td>Baby puddings</td>
<td>12.09</td>
</tr>
<tr>
<td>Baby soups, soup mixes</td>
<td>0.36</td>
</tr>
<tr>
<td>Baby meat dinners</td>
<td>4.56</td>
</tr>
<tr>
<td>Baby combination dinners</td>
<td>1.36</td>
</tr>
</tbody>
</table>
and by assuming that all products within a food category contained sucrose at the levels shown in Table I. Because of factors detailed in its report the NRC subcommittee believed that the estimated average intakes (Table II) are likely to be higher than would be the intakes achieved through consumption of a diet consisting totally of processed foods to which sucrose has been added at maximum levels. For example, the estimated daily intake of 31 g for infants in the 0-5 month age group includes 16 g contributed by infant formulas and would apply only to about 13 percent of this group who receive sucrose-containing formulas. Most infants in this age group are breast-fed or receive formulas in which the carbohydrate is lactose or corn syrup solids (9,10). However, the estimated possible average daily intake of 118 g for the 2-65+ year age group (Table II) is in good agreement with a per capita daily consumption of 127 g calculated from the 102.5 pound per capita per annum figure indicated for 1970 in Agricultural Statistics (7).

TABLE II
Possible Average Daily Intake of Added Sucrose by Age Group (8)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Intake</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g</td>
</tr>
<tr>
<td>0-5 mo</td>
<td>31</td>
</tr>
<tr>
<td>6-11 mo</td>
<td>59</td>
</tr>
<tr>
<td>12-23 mo</td>
<td>68</td>
</tr>
<tr>
<td>2-65+ yr</td>
<td>118</td>
</tr>
</tbody>
</table>

Calculated intake, g/kg body weight, is based on an average weight of 60 kg for an adult (11) and the following estimated weights of infants by age group: 0-5 mo, 5 kg; 6-11 mo, 8 kg; 12-23 mo, 11 kg (12).

IV. BIOLOGICAL STUDIES

Absorption, metabolism

Sucrose is largely absorbed in the small intestine after being hydrolyzed by a specific disaccharidase, sucrase, located in the brush border (13). There is also evidence that sucrose can be absorbed unchanged to a small extent, particularly at high dietary levels. This conclusion is based on the appearance of sucrose in the urine (14,15). Apparently sucrose, once absorbed in the blood stream, is restricted to the extracellular fluid and is excreted unchanged (16).
After sucrose is hydrolyzed in the brush border, glucose and fructose are actively absorbed into the portal circulation. Some of the fructose is converted to glucose in the mucosa; in animal species, conversions appear to vary between 10 and 70 percent (17,18). For man, conversions from 26 to 70 percent have been reported (19, 20).

The rate of absorption of the component monosaccharides appears to be a function of the form in which they are fed. Thus, serum fructose levels were higher in adult humans fed sucrose than when fed a mixture of glucose and fructose. Release of fructose by hydrolysis of sucrose within the brush border may facilitate absorption of fructose (21); also the furanose ring structure of fructose as released may be more readily absorbed than the equilibrium mixture of pyranose and furanose forms attained after being in solution for some time (22). There also appears to be a specific disaccharide effect on the induction of certain lipogenic enzymes in the rat liver by feeding sucrose or maltose as compared to feeding the component monosaccharides (23, 24).

Since nearly all ingested sucrose is absorbed as glucose and fructose, its metabolism is essentially that of these two monosaccharides. The metabolism of glucose and fructose has been discussed extensively (25, 26).

Evidence on the ability of dietary sucrose and fructose to modify serum and liver lipid patterns in animals is conflicting. Increased serum triglycerides, total liver lipid and serum cholesterol have been reported (27-32). However, these effects appear to depend upon several factors that may be summarized as follows:

1. Different animal species and different strains of the same species respond differently to the same dietary manipulation (33-36).

2. In general, cholesterol must be added to the diet to get hypercholesteremia when sucrose is fed (35, 37, 38). However, increased serum cholesterol with no added cholesterol in the diet has been reported (39).

3. Adaptation can occur with time so that the effects found in short-term experiments are decreased or disappear when the experimental period is lengthened (40).

4. The sex of the animals appears to play a role. Female rats show no changes under conditions that produce significant increases in serum lipid levels in male rats (41).
(5) Age of the animal is significant and more extensive effects are found in mature rats than young ones (42). On the other hand, sucrose feeding early in life has been reported to potentiate the effect later in life (43). The mechanism of these effects is not well defined and several hypotheses have been presented (44-47).

Similar conflicting results have been obtained in studies with man which have been reviewed in several papers (32, 48-50). Ahrens and his colleagues introduced the concept of carbohydrate-induced lipemia and suggested that carbohydrates, rather than lipids may have a dominant effect on atherosclerosis (51). Although the effect of carbohydrates on serum lipids has been confirmed, a variety of factors influence serum lipid levels. Not the least among these is the composition of the diet particularly in those experiments that show large differences in the effects of sucrose compared to starch (52-54). In these experiments, as much as 500 g of the test substances (cornstarch or sucrose) were fed daily. Other factors include age (55) and sex (56). On the whole, the effects of dietary carbohydrates on serum cholesterol in man appear to be less significant than those produced by the type and amount of dietary fat and these effects of carbohydrate are unlikely to be of importance within the normal range of diets consumed by man (57, 58). The effect of dietary carbohydrates on serum triglycerides, while more consistent, still appears of lesser significance than that produced by fat. Moreover, these changes appear to be of acute significance, longer periods of experimentation resulting in adaptation and return to initial values (59). These changes are consistent in that higher plasma triglyceride levels result from feeding high levels of sucrose as compared to starch (60). However, sucrose appears to have no greater effect than starch on serum triglyceride levels in normolipemic men in energy balance, when the level of sucrose in the diet is comparable to the average U.S. intake (58).

Sucrose feeding appears to be of greater significance in hyperlipemic individuals in that changes in serum cholesterol and triglycerides, particularly the latter, are more exaggerated when sucrose is added to or removed from the diet (61-63). In other experiments, these changes have been attributed to a synergistic effect of dietary sucrose and animal fat (64) or to the caloric level of the diet (65). Studies of free-living populations have indicated a prevalence of hypertriglyceridemia (serum triglycerides ≥ 200 mg per dl) up to 27 percent in adult males (66–68). Although several investigators have found elevated serum triglycerides to be associated with increased susceptibility to coronary artery disease (69 - 71), serum cholesterol level appears to be more significantly associated, and hypertriglyceridemia per se, except in women over 50, does not appear to be an independent risk factor in coronary artery disease (72-74). One study (69), however, indicated elevated serum triglycerides and cholesterol to be risk factors independent of each other. A firm association between sugar consumption and coronary artery disease has not been established (75).
Acute and chronic studies

The oral LD$_{50}$ (11 days) for sucrose given as a single dose by intragastric cannula has been estimated to be $35.4 \pm 7.0$ g per kg in adult male Wistar rats and $29.7 \pm 3.7$ g per kg in adult female Wistar rats (76). The clinical signs associated with this toxicity included hypokinesia, prostration, abdominal bloating, diarrhea and cyanosis. Deaths in the first 10 hours appeared to be due to gastroenteritis and capillary congestion of the brain and meninges. Increased urine volume also was noted.

Boyd and his colleagues also investigated the effect of several factors on the acute toxicity of sucrose (77). The following were found to modify the toxic response: volume of dose (in distilled water), sex, size of animal and dose schedule. The toxic effects appeared, in part, to result from the hyperosmotic nature of the test solutions and to the physical effects of large intragastric volumes, and not to be related to the toxicity of sucrose per se.

The oral LD$_{50}$ (100 days) for rats was estimated to be $28.5 \pm 1.3$ g sucrose per kg per day (78). The dose was administered daily by intragastric cannula to young male rats. Because all animals were fed a standard chow diet and caloric intake was the same in all groups, it is conceivable that these results were complicated by malnutrition of the test animals receiving the higher dose levels. This may explain the fact that considerably higher levels of sucrose often produce no toxic effects when fed as part of an experimental ration.

In another study the relative toxicities of several sugars, including sucrose, were estimated when fed as 80 percent of the diet to rats for 26 weeks (79). Although no deaths were observed, changes were found in organ weight, hepatic fat deposition and plasma cholesterol. Fructose produced the most marked changes and glucose the least; sucrose had an intermediate effect, presumably due to its fructose content.

Sucrose has been a component of experimental animal diets for many years in amounts ranging from 7 to 77 percent of the diet (80,81). Since these diets were fed to both control and test groups in the appropriate studies, no significant toxicological effects attributable to the sucrose component of the diet have been reported. It must be noted, however, that in none of these studies was the toxicity of sucrose itself under examination. One early report suggested that feeding high sucrose diets can result in reproductive failure in rats. In a two-year study, Whitnall and Bogart (82) found that sucrose but not lactose or starch, caused essentially complete reproduction failure when fed to female rats as 20 percent of the diet (about 10 g per kg body weight).
Several studies have suggested that feeding sucrose in place of starch can decrease life span in animals susceptible to kidney disease. Dalderup and Visser (83) reported a 21-week reduction in life span of male rats susceptible to nephritis when sucrose replaced 15 percent of the starch calories. In a similar experiment, Durand et al. (84) found no effect on life span from substituting sucrose for starch in a strain of rat not susceptible to kidney disease but a decrease was noted when a susceptible strain was tested.

Preliminary results indicate that supplementation of the diet with sucrose may cause a small increase in blood pressure. Mean diastolic pressure of 26 human volunteers increased from 73.4 ±1.3 mm Hg on their normal diets to 78.2 ±1.2 mm Hg when the normal diets were supplanted with 200 g sucrose. Composition of the total diet was not given (85).

Special studies

A. Carcinogenicity

A number of studies utilizing a variety of protocols have shown no evidence of carcinogenicity resulting from the administration of sucrose. No tumors were found when sucrose was injected intraperitoneally or subcutaneously in rats and mice for varying periods of time (86–88). Hueper (89) also found no evidence of carcinogenicity when rats and mice were injected subcutaneously with 25 percent sucrose solutions twice weekly for two years. In feeding studies in which sucrose was included in the diet at levels ranging from 10 percent for mice (90) to 77 percent for rats (80) (about 15 and 40 g per kg body weight, respectively), no increase in tumor incidence was found that could be attributed to the feeding of sucrose.

B. Teratogenicity

No teratogenic effects were noted in white New Zealand rabbits intubated with sucrose at levels up to 10 g per kg body weight per day during the 6th to 18th day of gestation. In addition to lack of teratogenic effect, no evidence of embryonecrosis was noted (91). In a similar study, no effect on nidation, fetal and maternal survival, and organogenesis was noted in mice and rats fed doses up to 1.6 g per kg per day for 10 days (92).

C. Atherosclerosis

Yudkin has proposed that the consumption of sucrose is an important factor in the etiology of coronary heart disease (93–100). In general, his hypothesis may be summarized as follows:

(1) Mortality rates due to cardiovascular disease in several countries are correlated with sucrose consumption.
(2) There is a dynamic relationship between increasing sucrose consumption and cardiovascular disease.

(3) Individuals with cardiovascular disease consume more sugar than normal persons.

(4) Sucrose induces hyperlipemia and hyperinsulinemia which in turn may influence cardiovascular disease.

While data can be presented to support each of these points, there are conflicting reports. For example, the consumption of sugar is high in several countries but the incidence of cardiovascular disease is low (50, 101). In addition, the relationship between individual sucrose intake and the incidence of cardiovascular disease has not been confirmed by other investigators (102-104). These workers noted a correlation of sucrose consumption with cigarette smoking which could lead to an apparent association between sucrose intake and cardiovascular disease. In a recent report, a Joint Working Party of the Royal College of Physicians of London and the British Cardiac Society concluded that there is no firm evidence linking sugar intake and coronary heart disease (75).

D. Diabetes

Several reports suggested an impaired glucose tolerance in rats (105) and humans (106) fed sucrose for several weeks. Feeding sucrose resulted in increasing and extending the hyperglycemic period while starch produced an opposite effect. In other experiments on human subjects high sucrose diets (up to 64 percent) caused an increase in insulin response in a standard glucose tolerance test (60). While these results suggest that long-term consumption of sucrose can result in a functional change in the capacity to metabolize carbohydrates and thus lead to diabetes mellitus recent reports tend to contradict this hypothesis. For example, Medalie et al. (107) concluded that diet was not significantly associated with the development of diabetes mellitus from a multivariate analysis of findings in a study of the development of the disease in 10,000 adult men. Obesity and peripheral vascular disease were significantly associated. Anderson et al. (108) reported improvement in glucose tolerance when high sucrose diets were fed. Brunzell et al. (109) reported improved glucose tolerance in diabetics fed high sucrose diets after or during insulin or oral sulfonylurea therapy. It is important to note that improved glucose tolerance occurs only when caloric intake is not increased. Thus, the primary effort in control of diabetes mellitus appears to be restriction in total caloric intake rather than restriction in carbohydrate intake (110, 111).

It may be noted that the Advisory Panel of the Committee on Medical Aspects of Food Policy (Nutrition) on Diet in Relation to Cardiovascular and Cerebrovascular Disease, Department of Health and Social Security, United
Kingdom, included in its 1974 report the recommendation that "the consumption of sucrose, as such or in foods and drinks, should be reduced, if only to diminish the risk of obesity and its possible sequelae" (112).

E. Dental caries

Dental caries is an infectious disease involving a multifactorial etiology that, in addition to the infectious organism, includes a susceptible target and an environment conducive to the growth of the infectious agent. The process begins with the production by cariogenic organisms such as Streptococcus mutans, of long chain polysaccharides (polyglucans) that adhere to the teeth, entrapping bacteria and forcing close contact between the cariogenic organisms and the tooth surface (113). These organisms also produce lactic and other acids that attack the enamel surface of the tooth, decalcifying and ultimately producing a hole in the surface (114). The primary substrate for the production of both plaque and organic acids is carbohydrate although other dietary factors such as phosphate (115) can modify this response. Several investigators have found sucrose to be the most cariogenic substance among sugars and foods tested in animal experiments (116-120). In other studies, however, glucose, fructose, and other sugars have been shown to be almost as cariogenic as sucrose when fed under controlled feeding conditions (121-124). Individuals with hereditary fructose intolerance who avoid all forms of sweets: chocolates, candies, cakes, pastries and other sucrose and fructose-containing foods have less dental caries than the general population (125). However, dental caries occur in populations who have never used sugar or any other processed foodstuff (126).

While the cariogenicity of sucrose appears to be well established in animal studies, the differences in feeding patterns and tooth structure between experimental animals and man are significant, thus raising the question of the role of sucrose in human caries experience. In an extensive human institutional study, the Vipeholm study (127), 436 adult inmates of a Swedish mental institution were studied for five years. Their diets were modified to contain various carbohydrates either as part of the meal or as between-meal snacks. The results of this study suggest that, as in experimental animals, sucrose is cariogenic to humans but the magnitude of this effect is a function of the amount of sucrose consumed, its form and the frequency of consumption. Cariogenicity increased when sucrose was in a "sticky" form that had a strong tendency to be retained on tooth surfaces. Moreover, when such foods were consumed as part of the meal, they were less cariogenic than if they were consumed as between-meal snacks. Sugar solutions produced no additional caries when fed as part of the meal while toffees (44 percent sucrose, 22 percent starch + dextrins, 12 percent maltose and 9 percent monosaccharides) fed between meals were most cariogenic.
The results of the Vipeholm study have been confirmed in a series of other institutional and retrospective studies (128-130). In general, these studies, reviewed recently by Bibby (131) suggest that the consumption of high-retention sucrose products between meals correlates well with increased dental caries experience.

Epidemiological studies have documented a decrease in incidence of dental caries in several European countries during wartime when supplies of sucrose were curtailed and an increase to prewar incidence after sugar again became available (132-134). However, from a review of data on caries experience in English children and young adults, Jackson concluded that the rise in consumption of sweets and sugars that followed World War II was associated with little or no increase in the incidence of dental caries (135). Also, it has been pointed out that the effect of restrictions on refined flour as well as sugar under wartime conditions in Europe and their replacement by other carbohydrate sources should not be neglected (136,137).

The recent increase in availability and consumption of presweetened cereals has raised the question of their potential cariogenicity. Several studies designed to test the effect of their consumption on dental decay have not revealed any increase in caries when compared to similar diets in which nonsweetened cereals were consumed (138-140). On the other hand, Shaw and his associates (141) obtained significant increase in caries in rats fed presweetened cereals as part of their diet. The difference between the studies may be a function of exposure since, in the human studies, the cereals were fed at only one meal each day while the rats were fed ad libitum.

The "nursing bottle syndrome" in children is characterized by rampant carious breakdown of the anterior maxillary teeth and occasionally the posterior mandibular teeth. This syndrome is attributed to the practice of placing bottles of sugar-containing solutions (including formulas) in the mouth of an infant at bedtime and allowing the infant to fall asleep with the bottle in his mouth (142-144). The result is the establishment of excellent conditions for the growth of oral flora and the formation of plaque. Some effort has been made to associate this syndrome with the consumption of milk. However, the results strongly suggest that most of the components of milk tend to be protective against caries and that the primary agent in this syndrome is the carbohydrate, either lactose or, more effectively, sucrose.

It is clear from the reports in the literature on dental caries that sucrose is among the most cariogenic substances. However, the magnitude of the effect is complex and depends on frequency of consumption, duration of exposure, the form in which the sucrose is fed and the nature of the other materials eaten with sucrose.
V. OPINION

Sucrose is the standard of naturally-occurring sweetness, joining other nutrients usually carbohydrate in nature, that comprise a group of palatable foodstuffs known to be relatively efficient sources of energy, simple in composition and rapidly metabolizable for utilization and storage. Sucrose has been used routinely since antiquity to improve the palatability of food preparations.

By all conventional tests, sucrose is a substance of extremely low acute toxicity. Consumption of sucrose in large amounts or at frequent intervals contributes to the development of dental caries. Overconsumption of sucrose probably contributes to obesity and possibly results in dietary imbalances and in modification of lipid metabolism which potentiates coronary heart disease. Tenuous relationships between sucrose ingestion and diabetes mellitus and other diseases also have been suggested. The possibility that sucrose may be involved in such deleterious effects continues to stir controversy, as is evident by the size of the scientific and popular literature on sugars in the human diet and the appearance of new research findings and concepts. Consequently, broad generalizations based upon the inconclusive evidence now available must be made and viewed with caution.

One of the important facts is that sucrose is both a significant natural constituent of food and a major additive to foods and beverages. It is commonly used as such by the consumer and added by food processors as a component of various foods. While per capita consumption of sucrose has changed little in the United States over the past 50 years, it is also true that about 70 percent of the per capita intake is now contributed by processed foods. This situation makes it difficult to exercise individual choice in the selection of a low sucrose diet.

Unlike most other foods, sucrose furnishes virtually only energy. While sucrose makes a substantial contribution to dietary caloric needs, in excessive amounts its effect on the intake of other nutrients may result in nutritional imbalances and, at least marginal, dietary deficiencies. Since over 15 percent of the per capita caloric intake of the population in the United States is from sucrose, it is likely that some individuals may eat enough to exclude adequate amounts of other foods that furnish required nutrients.

Findings linking ingestion of sucrose with diabetes are essentially circumstantial. There is no plausible evidence that sucrose, except as it is a non-specific source of excessive calories, is related to the disease. In those experiments in which impaired glucose tolerance was measured, highly distorted dietary patterns and excessive sucrose intakes were required.
The experimental evidence associating sucrose with cardiovascular
disease is also less than clear. It seems likely that the observed hyper-
lipidemic effects of high levels of sucrose in the diet of animals and man
are due primarily to its relatively rapid rate of hydrolysis and absorption
and that any differences between the metabolism of its hydrolytic products,
glucose and fructose, are of questionable significance. There is no evidence
that ingestion of sucrose in the concentrations that occur in the average diet
causes significant elevations in blood cholesterol or other lipids. Furthermore, it would appear that the primary dietary factors involved in cardio-
vascular disease are the nature and amount of fat in the diet. Thus, the
role of sucrose in cardiovascular disease appears to be secondary although
it may represent a potentiating factor in its etiology.

Of all the carbohydrates tested, sucrose is among the most cario-
genic. Individuals who assiduously avoid consumption of sucrose because
of an inborn error of metabolism — fructose intolerance — generally have
little or no dental caries. However, dental caries can and do occur in
people who have never used sugar or processed foods. Various factors
affect the cariogenicity of sucrose and other foods. These include frequency
and duration of exposure, age of the subject, and stickiness of the sugar or
materials with which it is consumed. Honey and figs, for example, are
highly cariogenic and pregelatinized starches also are conducive to the
development of dental caries. The significant effects of between-meal
eating on the frequency and severity of dental caries has been demonstrated.
Protection against dental caries is facilitated by limitation of the frequency
of consumption of sucrose and other cariogenic foods. Informing the con-
sumer of the sugar content of foods by appropriate labeling could lead to
judicious selection of sweetened foods. Choices could be made easier with
a greater selection of less sugared foods in the market place.

In light of all of the foregoing, the Select Committee concludes that:

1. Reasonable evidence exists that sucrose is a
contributor to the formation of dental caries
when used at the levels that are now current
and in the manner now practiced.

2. Other than the contribution made to dental
caries, there is no clear evidence in the
available information on sucrose that demon-
strates a hazard to the public when used at the
levels that are now current and in the manner
now practiced. However, it is not possible
to determine without additional data, whether
an increase in sugar consumption — that would
result if there were a significant increase in the

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total of sucrose, corn sugar,* corn syrup,* and invert sugar,* added to foods — would constitute a dietary hazard.

*Health aspects of corn sugar (dextrose), corn syrup, and invert sugar are evaluated in a report of the Select Committee (145).
VI. REFERENCES CITED


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141. Personal communication from Dr. J.H. Shaw, Harvard School of Dental Medicine to Dr. Sanford A. Miller (1975).


VII. SCIENTISTS CONTRIBUTING TO THIS REPORT

1. Members of the Select Committee on GRAS Substances:

Joseph F. Borzelleca, Ph.D., Professor of Pharmacology, Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, Va.

Harry G. Day, Sc.D., Professor Emeritus of Chemistry, Indiana University, Bloomington, Ind.

Samuel J. Fomon, M.D., Professor of Pediatrics, College of Medicine, University of Iowa, Iowa City, Iowa.

Bert N. La Du, Jr., M.D., Ph.D., Professor and Chairman, Department of Pharmacology, University of Michigan Medical School, Ann Arbor, Mich.

John R. McCoy, V.M.D., Professor of Comparative Pathology, New Jersey College of Medicine and Dentistry, Rutgers Medical School, New Brunswick, N.J.

Sanford A. Miller, Ph.D., Professor of Nutritional Biochemistry, Massachusetts Institute of Technology, Cambridge, Mass.

Gabriel L. Plaa, Ph.D., Professor and Chairman, Department of Pharmacology, University of Montreal Faculty of Medicine, Montreal, Canada.

Michael B. Shimkin, M.D., Professor of Community Medicine and Oncology, School of Medicine, University of California, San Diego, La Jolla, Calif.

Ralph G.H. Siu, Ph.D., Consultant, Washington, D.C.

John L. Wood, Ph.D., Distinguished Service Professor, Department of Biochemistry, University of Tennessee Medical Units, Memphis, Tenn.

George W. Irving, Jr., Ph.D. (Chairman), Research Associate Life Sciences Research Office, Federation of American Societies for Experimental Biology, Bethesda, Md.
2. LSRO staff:

C. Jelleff Carr, Ph.D., Director
Kenneth D. Fisher, Ph.D., Associate Director
Richard G. Allison, Ph.D., Research Associate
Samuel B. Detwiler, Jr., Research Associate
Andrew F. Freeman, Research Associate
Frederic R. Senti, Ph.D., Research Associate
John M. Talbot, M.D., Research Associate

The Select Committee expresses its appreciation to the following technical experts and organizations who contributed information and data:

Donald J. Forrester, Professor and Chairman, Dept. of Pediatric Dentistry, University of Maryland at Baltimore, School of Dentistry, Baltimore, Md. 21201.


Edmond G. Vanden Bosche, D.D.S., Associate Professor, Fixed Restorative Dentistry, University of Maryland, School of Dentistry, Baltimore College of Dental Surgery, Baltimore, Md. 21201.

Report submitted by:

October 5, 1976
Date

George W. Irving, Jr., Chairman
Select Committee on GRAS Substances
Four requests for a hearing were received and the following individuals made presentations.

Mr. Bendt Bladel, Technical Director, National Confectioners Association of the United States, 36 South Wabash Avenue, Chicago, Illinois 60603

Dr. Richard A. Ahrens, Professor, Food and Nutrition, Department of Food, Nutrition and Institution Administration, College of Human Ecology, University of Maryland, College Park, Maryland 20742

Frederick J. Stare, M.D., 665 Huntington Avenue, Boston, Massachusetts 02115

Dr. G. Norris Bollenback, Scientific Director, The Sugar Association, Inc., 1511 K Street, N.W., Washington, D.C. 20005

The following individuals submitted material in lieu of appearance at the hearing.

David R. Bassett, M.D., Associate Professor of Internal Medicine, University Hospital, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan 48109

Drs. Bela Szepesi, Research Chemist, Otho E. Michaelis, IV, Research Nutritionist, and Sheldon Reiser, Chief, Carbohydrate Nutrition Laboratory, Nutrition Institute, Agricultural Research Center, U.S. Department of Agriculture, Beltsville, Maryland 20705