EVALUATION OF THE HEALTH ASPECTS OF SORBOSE
AS A FOOD INGREDIENT

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Prepared for

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

Contract No. FDA 72-85
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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 of evaluations of the health aspects of the Generally Recognized as Safe (GRAS) or prior sanctioned food substances being made by the Federation of American Societies for Experimental Biology (FASEB) under contract no. 72-85 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
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I. INTRODUCTION

This report evaluates the health aspects of using sorbose as a food ingredient. The evaluation has been based partly on the information contained in a scientific literature review (monograph) furnished by FDA (1), which summarizes the world's scientific literature from 1920 through 1970.* 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 recognized as 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 of December 19, 1974 (39 FR 43865 & 43866) 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 sorbose as a food ingredient. The Select Committee received no requests for such a hearing on sorbose.

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 21 CFR 121.1, revised April 1, 1974 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 these substances in full recognition of the foregoing provisions. In reaching its conclusions on safety the Select Committee, in accordance with FDA's guidelines, is relying primarily on the absence of

*The document is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
substantive evidence of, or reasonable grounds to suspect, a significant risk to the public health, and realizes that a conclusion based on such reasoned judgment is expected even in instances where the available information is qualitatively or quantitatively limited. The 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 sorbose 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

Sorbose, a sweet crystalline ketohexose, is soluble in water and nearly insoluble in alcohol. It was originally identified in the juice of mature berries from the mountain ash (Sorbus aucuparia) where it occurs as the result of microbial oxidation of sorbitol (2). L-sorbose can be prepared by the catalytic hydrogenation of glucose and the oxidation of the resulting D-sorbitol by Acetobacter suboxydans (3).

The Code of Federal Regulations lists sorbose as GRAS as a substance migrating to food from cotton and cotton fabrics used in dry food packaging (4). The Food Chemicals Codex provides no specifications for sorbose as used in this manner (5). Commercially, the principal use of sorbose is in the production of ascorbic acid by a variety of processes in which both chemical and microbial techniques are used (6).

III. CONSUMER EXPOSURE DATA

The Select Committee on GRAS Substances has no data on the amounts of sorbose occurring in packaging materials or used as an ingredient in the treatment of packaging materials. However, the Select Committee believes that the total amount of sorbose consumed as a result of its migration from dry food packages is extremely small.
IV. BIOLOGICAL STUDIES

No studies have been directed primarily toward determining the health aspects of the long term use of sorbose as a food ingredient. Inferences on the health aspects of sorbose consumption at its present level may be drawn from reports on its absorption and metabolism by animals and man.

Although certain sugars, such as glucose and galactose, are transported through the hamster's small intestine in vitro against a concentration gradient, sorbose and such sugars as fructose and mannose are not so transported (7). In isolated guinea pig small intestine, sorbose enters the intestine by diffusion (8). As determined in dogs via fistulas in the small intestine, the rate of absorption is directly proportional to the lumen concentration (9). The decrease in serum inorganic phosphate exhibited in dogs following intravenous injection of 1 ml per kg of a 3 molar solution of L-sorbose (about 540 mg per kg of body weight), was similar to the decrease observed when D-glucose was injected (10).

In a series of ten tests ancillary to biochemical experiments, rats fed a single dose of 13 g of sorbose per kg showed no toxic symptoms. Sorbose was converted to glycogen in the liver when fed to fasted rats for 120 hours at 33 percent of a basal fat diet (11). Studies on the biosynthesis of ascorbic acid indicated that sorbose is not a direct intermediate as suggested by molecular structure, but is first converted to glucose, then to ascorbic acid (12, 13). A ketokinase with a high affinity for sorbose has been identified in rat intestine (14) and beef liver (15). When fed in drinking water, sorbose did not sustain the weight of hypophysectomized rats as did glucose, and it was not absorbed as rapidly from the intestine (16).

Both healthy and diabetic human subjects absorbed sorbose from the gastrointestinal canal as rapidly as glucose. Sorbose excretion in the urine after 50 g per os in 500 ml of water was nearly complete after six hours and amounted to 14 percent of the dose. At an increased intake (100 g per os in 500 ml) approximately 12 percent of the dose was excreted in six hours (2). A study of the resorption and net metabolism of D-fructose, L-sorbose and sorbitol in healthy and in hereditary fructose intolerant infants showed that the utilization of sorbose was significantly reduced in the intolerant infants (17).

No studies have come to the Select Committee's attention on carcinogenicity related to orally administered sorbose. However, in one study, designed to test the carcinogenicity of eight hypertonic sugar
solutions including sorbose, the subcutaneous injection of 60 C57BL mice and 60 Bethesda rats with 0.5 and 2.0 ml, respectively, of a 25 percent solution of sorbose (250 mg per ml) in the nape of the neck two or three times a week for up to two years resulted in two rats developing sarcomas at the site of injection after 21 months (18). The author and a subsequent reviewer (19), concluded that sorbose and presumably other sugars should not be regarded as carcinogenic on the basis of this experiment.

V. OPINION

The results of sorbose-feeding tests with fasted rats showed no acute toxic effects for sorbose given in excess of potential human dietary exposure. The metabolic products of sorbose metabolism in animals do not appear to include toxic substances and the chemical structure of sorbose does not suggest potential hazards. The results of the only study of the carcinogenicity of sorbose, involving parenteral administration in rats, have been judged by the investigator and reviewers to be negative.

Based on these considerations, and the fact that sorbose is permitted only as an ingredient of cotton fabrics used in dry food packaging, the Select Committee concludes that:

There is no evidence in the available information on sorbose that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when it is used at levels that are now current or that might reasonably be expected in future.
VI. REFERENCES CITED


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Report submitted by:

February 28, 1975
Date

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