EVALUATION OF THE HEALTH ASPECTS OF HYDROSULFITES AS THEY MAY MIGRATE TO FOODS FROM PACKAGING MATERIALS

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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 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.

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I. INTRODUCTION

This report concerns the health aspects of using hydrosulfites as ingredients of food packaging materials. It 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 1973.* 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, an announcement was made in the Federal Register of April 22, 1976 (41 FR 16848 and 16849) 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 hydrosulfites as ingredients of food packaging materials. The Select Committee received no requests for such a hearing on hydrosulfites.

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, 1975, 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

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*The document (PB-228 551/8) is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
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 hydrosulfites and submits its interpretation and assessment in this report, which is intended for the use of FDA in determining the future status of these substances under the Federal Food, Drug, and Cosmetic Act.

II. BACKGROUND INFORMATION

Sodium hydrosulfite, Na₂S₂O₄, and zinc hydrosulfite, ZnS₂O₄, are free-flowing white powders that are extremely soluble in water. In air, especially moist air, both are rapidly oxidized to bisulfites and bisulfates. In dilute solutions hydrosulfites decompose, with the formation of sulfur dioxide and colloidal sulfur (1-4).

Metal hydrosulfites (dithionites) are used commercially as reducing agents in polymerization processes and textile manufacturing, and for bleaching wood pulp, soap, sugar, molasses, glue, and oils and fats (2). Issue of a U.S. patent in 1940 for sodium hydrosulfite as an antioxidant in beer did not result in its general use, partly because of its instability in dilute solutions, especially under slightly acid conditions; sodium isoascorbate with the sodium hydrosulfite was used to overcome this instability (4). Desired protection of beer was achieved when the sodium hydrosulfite-sodium isoascorbate mixture (1:3) was used at a level of 40 ppm. In beer and other aqueous systems, the hydrosulfite rapidly changes to sulfite. Apparently the antioxidant mixture is rarely, if ever, used in beer today.

Experiments carried out in Spanish trawlers showed that treatment of frozen and ice-stored crustaceans with sodium hydrosulfite solutions prevented black spot (5). According to information obtained from the National Marine Fisheries Service, Department of Commerce, sodium hydrosulfite is not used on crustaceans consumed in the United States.
Hydrosulfites have not been approved for use as direct food ingredients, and no standards for them are listed in the Food Chemicals Codex (6). However, both sodium and zinc hydrosulfites are generally recognized as safe as substances migrating to food from paper and paperboard products used in food packaging under the provisions of the Code of Federal Regulations (7).

III. CONSUMER EXPOSURE DATA

The Select Committee has not been successful in finding data that would provide an adequate basis for estimating the extent to which the hydrosulfites contained in paper and paperboard migrate to food from packages and containers. A National Research Council subcommittee report (8) does not include consumer exposure data for materials from this source that may be present in food. The Select Committee has found only one study that could be somewhat indicative of the magnitude of migration of chemicals from paper containers. Davison et al. (9) studied the migration of rosin components from sized paper to foods and concluded that foods stored up to several weeks in such packaging materials contain on the average, no more than 7 ppm of rosin. The papers used contained up to 7 percent rosin.

The Code of Federal Regulations (7) in Section 21 CFR 121.101(h) does not specify the nature of the foods packaged, whether dry or moist, fatty or fat-free; nor does it specify the nature of the paper product, whether coated, impregnated, or calendared. It must be assumed that any combination of these conditions can prevail and that it is the intent of the present regulation to confer GRAS status on the hydrosulfites when used under any of these conditions.

In this regard, consideration of an aspect of papermaking technology is relevant. It seems likely that most of the hydrosulfites added in the papermaking process would be converted to sulfites or sulfates and removed, together with any residual hydrosulfite, in the washing and pressing operations on the papermaking machine.

In light of these considerations, it would appear that the amount of hydrosulfites that might be present in the paper used for food packaging would be small, and the amount that might migrate from such packages into food is likely to be extremely small.
IV. BIOLOGICAL STUDIES

Acute toxicity

Oral administration of up to 1 g sodium hydrosulfite per kg body weight to dogs was without any apparent untoward effect, except that in many instances vomiting occurred (10). Details of the tests were not given. Rats showed no adverse reactions to intravenous injections of 25 to 50 mg per kg sodium hydrosulfite (11). At 100 mg per kg, labored breathing appeared during the actual injection and persisted for 5 to 10 minutes, followed by recovery. At 150 mg per kg, labored breathing increased markedly with signs of suffocation; however, doses as high as 210 mg per kg, although temporarily incapacitating, were not lethal. An intravenous dose of 240 mg per kg was fatal in 5 minutes. In a second series of tests, rats survived intravenous doses of 125 mg per kg, but succumbed to 150 mg per kg in 7 minutes.

A 10 percent sodium hydrosulfite solution administered at levels of 100 mg per kg by stomach tube was effective in preventing fatal arsenical poisoning in dogs (10). When given within 10 minutes after administration of a fatal dose of arsenic, 90 percent of the animals survived. No apparent adverse effects resulted from the oral administration of the sodium hydrosulfite solution.

A 5 percent solution of sodium hydrosulfite reduced the rate of natural mutagenesis by more than tenfold in an unstable heredity strain of Bacterium prodigiosum (12).

No short- or long-term feeding studies or studies of possible carcinogenicity or teratogenicity of the hydrosulfites have come to the attention of the Select Committee, and no reports were found concerning absorption, distribution, metabolism, and excretion of these substances. However, since hydrosulfites are converted readily to bisulfite, bisulfate or sulfur dioxide in air or aqueous solution, absorption and metabolism of these compounds would be expected to be similar. The sulfiting agents will be evaluated in a forthcoming report of the Select Committee (13); evaluation of the sulfates has been completed (14).

While no specific information on the toxicity of zinc hydrosulfite was available to the Select Committee, a number of other zinc salts, such as zinc carbonate, and zinc sulfate, have been evaluated (15) and found to be without adverse effects in doses approximating 50 mg per kg body weight per day. Such doses greatly exceed those that would result from migration of zinc hydrosulfite into foods from paper or paperboard packaging materials.
V. OPINION

Information on the toxicity of sodium hydrosulfite is extremely limited. Nevertheless, the available data indicate that the oral administration of up to 1 g of the sodium salt per kg body weight does not cause significant harm in dogs, and the intravenous injection of 25 to 50 mg per kg has resulted in no apparent ill effects in rats. These doses are many orders of magnitude greater than those that could result from the consumption of foods packaged in sodium hydrosulfite-containing paper and paperboard packaging materials.

Because zinc compounds, such as the carbonate and sulfate do not elicit adverse effects when administered orally to experimental animals at levels of 50 mg per kg., and sodium hydrosulfite is without apparent adverse effects at equivalent levels it is reasonable to conclude that zinc hydrosulfite would react similarly.

In the light of these considerations, the Select Committee concludes that:

There is no evidence in the available information on sodium hydrosulfite and zinc hydrosulfite that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used in food packaging materials as now practiced or as they might reasonably be expected to be used for such purposes in the future.
VI. REFERENCES CITED


8. Subcommittee on Review of the GRAS List (Phase II), 1972. A comprehensive survey of industry on the use of food chemicals generally recognized as safe (GRAS). Prepared under DHEW contract FDA 70-22 by Committee on Food Protection, Division of Biology and Agriculture, National Research Council, National Academy of Sciences, Washington, D.C.


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