EVALUATION OF THE HEALTH ASPECTS OF CALCIUM OXIDE AND CALCIUM HYDROXIDE AS FOOD INGREDIENTS

1975

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
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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 calcium oxide and calcium hydroxide as food ingredients. It has been based partly on the information contained in a scientific literature review (monograph) furnished by FDA (I), 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 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 of August 29, 1975 (40 FR 39917 and 39918) 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 calcium oxide and calcium hydroxide as food ingredients. The Select Committee received no requests for such a hearing on calcium oxide and calcium hydroxide.

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 with FDA's guidelines, is relying primarily on the absence of substantive evidence of, or reasonable grounds to suspect, a significant risk to the

*The document (PB-223 851/7) is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
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 calcium oxide and calcium hydroxide 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

Food-grade calcium oxide, CaO, and calcium hydroxide, Ca(OH)₂, are used in foods under the provisions of the Code of Federal Regulations (2). Calcium hydroxide is GRAS as a miscellaneous and/or general purpose food additive [121.101(d)(8)] and as a substance migrating to food from paper and paperboard products used in food packaging [121.101(i)]; it is separately regulated [51.1] and may be used as an optional ingredient in canned peas to modify alkalinity. Calcium oxide is GRAS for use as a nutrient and/or dietary supplement [121.101(d)(5)], and as a miscellaneous and/or general purpose food additive [121.101(d)(8)].

Calcium oxide (lime) readily absorbs carbon dioxide and water from the air. It is soluble in water forming Ca(OH)₂, generating heat in the process. It is soluble in glycerol but is insoluble in alcohol. It is used in food for pH control, and as a texturizing, firming, and anticaking agent. Calcium hydroxide (slaked lime) is an alkaline, slightly bitter-tasting white powder which readily absorbs carbon dioxide to form calcium carbonate. When heated it loses water, leaving calcium oxide. It is slightly soluble in water; the pH of a saturated aqueous solution at 25°C is 12.4. Its most frequently reported use is as a pH control agent (3).

Specifications for food-grade calcium oxide and calcium hydroxide include the following limits of impurities (4): arsenic, not more than 3 ppm; fluoride, not more than 50 ppm; heavy metals (as lead), not more than 40 ppm; and lead, not more than 10 ppm. Calcium oxide must assay not less than 95 percent CaO after ignition, and loss on ignition must not exceed 10 percent. Calcium hydroxide must assay at least 95 percent Ca(OH)₂. Magnesium and alkali salts are limited to 3.6 percent for calcium oxide and 4.8 percent for calcium hydroxide.
A subcommittee of the National Research Council (NRC) surveyed manufacturers in 1970 concerning the usual and maximal addition of calcium oxide and calcium hydroxide to foods and estimated the possible average daily intake of these substances for various age groups (5). Based on information supplied by those manufacturers who reported adding the substance to at least one food in a category, weighted means were calculated for the usual and maximal addition of the substance to foods in the category. For a given category, the mean of the usual 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. Weighted means of the usual level of addition of calcium oxide and hydroxide are given in Table I. The Select Committee has no information concerning any changes in the level of addition of calcium oxide and calcium hydroxide to foods in recent years.

The NRC subcommittee estimated possible average daily intakes (Table II) from Market Research Corporation of America data on the mean frequency of eating foods by food category, U.S. Department of Agriculture data on mean portion size of foods in these categories and the assumption that all food products within a category contain the substance at the level shown in Table I. Such an assumption is likely to lead to overestimates of intake. The NRC subcommittee has recognized that in most cases its calculations of possible intakes are overstated, often by considerable margins.* Because of factors detailed in Section XI of the subcommittee's report (5) they stated that the possible average estimated total dietary intakes are likely to be much higher than would be the intakes achieved through consumption of a diet consisting totally of processed foods to which the substances had been added at the maximum levels.

In the use of calcium hydroxide in foods, manufacturing practices appear to vary widely at least in such food categories as grain products (pastas and rice dishes), dairy product analogs and baby formulas. Thus, it is not surprising that the usual concentration of calcium hydroxide in a

*An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations" of the NAS subcommittee's report (5). The Select Committee finds this explanation reasonable, and concurs in the first recommendation in Section XII of the same report, that "In order to conduct a more accurate survey on the intake of substances used in food processing, food consumption data collected specifically for this purpose are needed."
TABLE I

Level of Addition of Calcium Hydroxide and Calcium Oxide to Foods by Food Category (5)

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Calcium oxide Weighted mean percent</th>
<th>Calcium hydroxide Weighted mean percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grain products such as pastas or rice dishes</td>
<td>0.04</td>
<td>0.90</td>
</tr>
<tr>
<td>Milk, milk products</td>
<td>0.06</td>
<td>***</td>
</tr>
<tr>
<td>Frozen dairy desserts mixes</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Processed fruits, juices and drinks</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Condiments, relishes, salt and substitutes</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Soft candy</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sweet sauces, toppings, syrups</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Soups, soup mixes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Snack foods</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Beverages, nonalcoholic</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>Beverages, alcoholic</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Reconstituted vegetable proteins</td>
<td></td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Dairy products analogs</td>
<td>0.44</td>
<td></td>
</tr>
<tr>
<td>Instant coffee and tea</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Baby formulas</td>
<td>0.04</td>
<td></td>
</tr>
</tbody>
</table>

Blanks in the table mean that the substance is not added to the foods indicated; asterisks (***)) in the table mean that (a) the substance is used in a processing phase of the foods indicated but residual levels in the final food product are negligible or unknown, or (b) the substance is used in the foods indicated but usage levels were not furnished by industry, or (c) the substance is in the foods indicated but the levels were considered to be reported incorrectly. Level of addition of calcium hydroxide and calcium oxide is the weighted mean of the levels reported by manufacturers as their usual addition to one or more products in a food category. For discussion of weighted mean see text, also Section X and Exhibit 50 of reference 5.
food category, as reported in Table I is unsuitable for estimating average or 50th percentile intakes. The Select Committee believes the average intakes calculated by the NRC subcommittee (Table II) could be achieved only by a small fraction of the population.

**TABLE II**

<table>
<thead>
<tr>
<th>Substance</th>
<th>0-5 months</th>
<th>6-11 months</th>
<th>12-23 months</th>
<th>2-65+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Oxide</td>
<td>3 1</td>
<td>40 5</td>
<td>39 4</td>
<td>37 1</td>
</tr>
<tr>
<td>Calcium Hydroxide</td>
<td>140 28</td>
<td>127 16</td>
<td>169 15</td>
<td>275 5</td>
</tr>
</tbody>
</table>

*Calculated intake, mg/kg body weight, was based on an average weight of 60 kg for an adult (6) and the following estimated weights of infants by age groups: 0-5 mo, 5 kg; 6-11 mo, 8 kg; and 12-23 mo, 11 kg (7).*

Average intakes are more likely to approximate the per capita intake calculated from the quantities used annually in foods (Table III). This is particularly evident from comparison of the estimate of average intake by the NRC subcommittee of 275 mg of calcium hydroxide daily by individuals over 2 years old (Table II) with the per capita consumption of 9 mg per day based on the amount used in food in 1970 (Table III). The Select Committee believes that the figure given in Table III represents a reasonable estimate of average daily consumption of calcium hydroxide by individuals over 2 years old. This view is supported by the following calculation: an addition of 0.9 percent calcium hydroxide to grain products (Table I) would result in addition of 486 mg of calcium per 100 g of product. This is severalfold higher than the total calcium concentration of most such products listed in standard tables of food composition (8).

In individuals less than 2 years old, average intakes of calcium hydroxide also appear to be overestimated in Table II. In the case of infants less than 6 months old, the overestimates result from the value given (Table I) as the usual addition to baby formulas. On any specified day, if one considers as a group all individuals less than 6 months old, it may be estimated that 60 percent will receive commercially-prepared infant formulas, the remainder being breastfed or receiving fresh or evaporated milk (9). Approximately 9 percent of all infants less than 6 months old receive milk-free commercially prepared infant formulas, mostly soy-isolate-based (10). A few such formulas contain calcium hydroxide.
TABLE III

Consumption of Calcium Oxide and Calcium Hydroxide
Based on Total Quantity Used Annually in Foods (5)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Relative amounts used$^{1}$ 1970/1960</th>
<th>Total used 1970$^{2}$ kg</th>
<th>Per capita daily intake$^{3}$ mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium Oxide</td>
<td>5.1</td>
<td>7,800,000</td>
<td>104</td>
</tr>
<tr>
<td>Calcium Hydroxide</td>
<td>2.1</td>
<td>660,000</td>
<td>9</td>
</tr>
</tbody>
</table>

$^{1}$ Based only on the reports from those respondents to the NRC survey who submitted information for both 1960 and 1970 (5).

$^{2}$ Total usage is based on the sum of kilograms used in foods as supplied by NRC (National Research Council) and FEMA (Flavoring Extract Manufacturers' Association) recalculated to 100 percent from survey data that the NRC subcommittee estimated to represent about 60 percent of the actual usage.

$^{3}$ Based on a U.S. population of 205 million.

In the case of calcium oxide, the NRC subcommittee's estimate of daily intake by individuals more than 2 years old is 37 mg (Table II). The per capita daily intake of calcium oxide calculated from the quantity used (Table III) was 104 mg per day. The Select Committee is unable to determine which of these estimates is the more nearly valid.

In its evaluation of calcium oxide and calcium hydroxide, the Joint FAO/WHO Expert Committee on Food Additives (11) states, "Provided the nutritional implications of the overall dietary intake of cations derived from these additives are taken into account, there appear to be no toxicological grounds to limit their use in accordance with good manufacturing practice." The Select Committee has considered the calcium:phosphorus ratio and the interaction of calcium with other components of the diet in its report on phosphates (12).

IV. BIOLOGICAL STUDIES

The Select Committee has found no reports of experiments specifically designed to determine the toxicity, mutagenicity, teratogenicity, or
carcinogenicity in relation to short-term or long-term feeding of calcium oxide. Similar reports are also unavailable on calcium hydroxide, with the exception of a report (13) on acute toxicity in the rat. In the absence of specific studies, there is no reason to suspect calcium as supplied by these two compounds would be different with respect to absorption and metabolism than calcium from other inorganic calcium compounds used as nutrients (12).

Because the food uses of calcium hydroxide cannot result in the exposure of animals and man to the caustic action of saturated or unbuffed calcium hydroxide solutions, most reports of the exposure of biological systems to such solutions are not relevant to an evaluation of the health aspects of the use of calcium hydroxide in foods.

The oral LD₅₀ in rats for calcium hydroxide has been reported (13) as 7,340 mg per kg body weight (range: 4,830 to 11,140 mg per kg body weight). The calcium hydroxide was administered in water (100 mg per ml) which is greatly in excess of its solubility (1.85 mg per ml water at 0°C)(14). Since calcium oxide forms calcium hydroxide in aqueous solution, its acute toxicity should be similarly low if the pH is controlled as it is when used in food.

Negative results were reported in one test for carcinogenicity of solid calcium hydroxide applied to hamster cheek pouches (15). Hamster cheek pouches were treated with 250 mg of calcium hydroxide per day for five days a week for two weeks; treatment was reduced to three times a week between the 2nd and 40th weeks of treatment. Six animals were treated for 81 weeks. All of the hamsters developed pouch lesions; three of the lesions progressed to distinct cellular atypia. Small foci of atypical cells in the squamous epithelium showed loss of cellular polarity and cells in the basal layer were hyperchromatic and fusiform. The authors "did not consider that these lesions were preinvasive cancer." The hamsters lived their normal lifespans without developing frank neoplasia.

The use of calcium oxide for the treatment of maize (lime-treated maize) causes some degradation of nicotinic acid, riboflavin, and thiamin, but the proportion of the total nicotinic acid in an available form is increased (16). This problem was studied in relation to the pellagragenic properties of maize. The nutritive deficiency of the treated maize manifested itself in rats in the form of growth rate depression. The rate depression, when compared to maize-fed controls receiving a vitamin B supplement, was reversed by the addition of riboflavin to the diet, or partially reversed by adding thiamin.

Calcium hydroxide is effective in reducing the growth-depressing activity of two percent tannic acid fed in a basal diet to day-old chicks if the calcium hydroxide (0.087 percent) is first mixed as a slurry with the
tannic acid (17). The authors speculated that under the alkaline conditions tannic acid and naturally present phenolic compounds were oxidized to less toxic compounds.

V. OPINION

Calcium oxide and calcium hydroxide as used in foods contribute to the total biologically available dietary calcium. No evidence has been found that demonstrates these compounds have adverse nutritional implications in the overall dietary intake of cations. Thus, normal physiological mechanisms that control calcium metabolism allow man to utilize these sources of calcium.

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

There is no evidence in the available information on calcium oxide and calcium hydroxide that demonstrates or suggests reasonable grounds to suspect a hazard to the public when they are used as direct or indirect food ingredients at levels that are now current or that might reasonably be expected in the future.
VI. REFERENCES CITED


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