EVALUATION OF THE HEALTH ASPECTS OF HYDROCHLORIC ACID AS A FOOD INGREDIENT

1979

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
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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.

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FASEB
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I. INTRODUCTION

This report concerns the health aspects of using hydrochloric acid as a food ingredient. 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 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; recent literature searches by the Toxicology Information Response Center, Oak Ridge, Tennessee; 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 January 12, 1979 (44 FR 2687-2690) 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 hydrochloric acid as a food ingredient. The Select Committee received one request for such a hearing but this request was withdrawn.

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 Act and in the Code of Federal Regulations (2) [21 CFR 170.3 and 170.30] 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. These sections of the Code also indicate 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 (2) recognizes further [21 CFR 170.30] 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 Committee, in accordance with FDA's guidelines, is relying primarily on the absence of substantive evidence

*The document (PB 241-962/0) is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
of, or reasonable grounds to suspect, a significant risk to the public health. While the 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 Committee there are insufficient data upon which to base a conclusion. The Committee is aware that its 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 hydrochloric acid 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

Hydrochloric acid (HCl) is GRAS [21 CFR 182.1057] under the Code of Federal Regulations (2) when "used as a buffer and neutralizing agent in accordance with good manufacturing practice." In addition, food starch may be acid-modified by treatment with hydrochloric acid under 21 CFR 172.892; hydrochloric acid may be added in such amounts as to reach pH 4.5 to 4.7 in the preparation of dry curd cottage cheese [21 CFR 133.129], tomato paste [21 CFR 155.191] and tomato puree [21 CFR 155.192]; tomato catsup [21 CFR 155.194] may be adjusted with hydrochloric acid during preparation to a pH no lower than 2.0 ± 0.2 with subsequent neutralization by alkali to 4.2 ± 0.2. Hydrochloric acid also is used in adjusting pH in brewing and as a hydrolytic agent in the manufacture of sodium glutamate, gelatin, and corn syrup (3). In most of its uses as a hydrolytic agent, the products of neutralization are removed. When used to adjust the acidity of food, the acid is neutralized or converted to salts by alkaline compounds present in foods. Foodstuffs to which hydrochloric acid has been added expose consumers predominantly to chloride ions and other chemical products resulting from its reaction with neutralizing agents or chemicals in the food. Free hydrochloric acid would be expected to be present in only minute amounts, if at all. Separate reports of the Select Committee have been or are being prepared on some of the chlorides, e.g., zinc chloride (4), ferric chloride (5), calcium chloride (6), sodium chloride and potassium chloride (7).

Hydrochloric acid exists as aqueous solutions of hydrogen chloride of varying concentrations. Concentrations of the acid commercially available are usually expressed in Baumé degrees (°Bé) from which percentages of hydrochloric acid and specific gravities are derived. Concentrations above 8.5° Bé (12.5 percent) fume in moist air, lose hydrogen chloride, and create a corrosive atmosphere. The pH of 1.0 N HCl is approximately 0.1 (1).

Hydrochloric acid is specified in the Food Chemical Codex (8) to contain not less than the minimum or within the range of Baumé degrees and concentration claimed or implied by the vendor, to have a specific gravity not less than the minimum or within the range specified or implied by the vendor, and to contain not more than 1 ppm arsenic, not more than 5 ppm heavy metals as lead, and not more than 5 ppm iron.

Hydrochloric acid has been found in minute amounts in the waters of some rivers and in volcanic areas. It is not present as such in plants. It occurs in the gastric juice of animals; the gastric juice of man contains about 0.5 percent of the acid (1).

A Joint FAO/WHO Expert Committee on Food Additives in 1966 and 1967 stated that hydrochloric acid is not regarded as a toxic substance in the concentrations are are used in food technology (9, 10).
III. CONSUMER EXPOSURE DATA

A National Research Council (NRC) subcommittee surveyed manufacturers in 1970 concerning the level of addition of the GRAS substances to foods. Based on information supplied by those manufacturers who reported adding hydrochloric acid 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 (Table I).

The NRC subcommittee has estimated possible average daily intakes of hydrochloric acid for various age groups (Table II) from data collected by the Market Research Corporation of America on the mean frequency of eating foods by food category, data on mean portion size of foods in those categories from the U.S. Department of Agriculture, and the assumption that all food products within a category contain hydrochloric acid at the levels 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, it was 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 substance had been added at the maximum levels. Thus, the Select Committee concludes that the estimates in Table II (30 mg per person per day for individuals over 2 years of age) are almost certainly excessive.

For most substances, the average daily per capita intake can be estimated from the total quantity used by the food industry. Such an estimate is given in Table III for hydrochloric acid and amounts to a per capita consumption of 378 mg per person per day. Much hydrochloric acid used in food processing (e.g., for hydrolytic purposes) is not included in Table I and therefore is not included in the estimates in Table II. Thus, the discrepancy in estimates between Tables II and III is understandable. While the value of 378 mg per capita per day may be approximately correct for the amount of hydrochloric acid used in food processing, actual per capita consumption of hydrochloric acid from foods is considerably less than 378 mg per day, and is likely to be less than the 30 mg per day given in Table II. A considerable portion does not remain in food, being left in processing liquors or neutralized in the food products.
TABLE I

Level of Addition of Hydrochloric Acid to Foods by Food Category (11)

<table>
<thead>
<tr>
<th>Food category</th>
<th>Weighted mean percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baked goods, baking mixes</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Cheese</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Processed fruits, juices and drinks</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Sweet sauces, toppings, syrups</td>
<td>0.273</td>
</tr>
<tr>
<td>Gelatins, puddings, fillings</td>
<td>***</td>
</tr>
<tr>
<td>Beverages, nonalcoholic</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Reconstituted vegetable proteins</td>
<td>***</td>
</tr>
<tr>
<td>Baby formulas</td>
<td>***</td>
</tr>
</tbody>
</table>

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 hydrochloric acid 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 11.
TABLE II

Possible Daily Intake of Added Hydrochloric Acid by Age Group (11)*

<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>Hydrochloric acid</td>
<td>1</td>
<td>6</td>
<td>15</td>
<td>30</td>
</tr>
</tbody>
</table>

*It should be noted that the figures in this table represent amounts of hydrochloric acid added to foods for pH adjustment during processing and not the amounts consumed as such. The acidic properties of this substance are well known. However, only minute amounts of hydrochloric acid per se remain in foods as ingested, since the acid is converted to neutral salts during processing by reaction with food components.

TABLE III

Quantity of Hydrochloric Acid Used by the Food Processing Industry and Calculated Per Capita Daily "Consumption" (11)

<table>
<thead>
<tr>
<th>Substance</th>
<th>Relative amounts used^</th>
<th>Total quantity added 1970¹</th>
<th>Per capita daily consumption^</th>
<th>mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochloric acid</td>
<td>9.1</td>
<td>29,000,000^</td>
<td>378</td>
<td></td>
</tr>
</tbody>
</table>

^Based only on the reports from those respondents to the National Research Council (NRC) survey who submitted information for both 1960 and 1970 (11).

¹Total usage is based on the sum of kilograms used in foods as supplied by the NRC subcommittee and by the Flavor and Extract Manufacturers' Association (FEMA) recalculated to 100 percent from survey data that the NRC subcommittee estimated to represent about 60 percent of the actual usage.

^Based on total consumption 1970 and a U.S. population of 205 million.

^A NRC resurvey (40) indicated that 37 million kg were used in 1975.
IV. BIOLOGICAL STUDIES

Absorption, metabolism, excretion

The human stomach normally contains sufficient hydrochloric acid, secreted by the parietal cells of the gastric glands, to maintain the pH of gastric juice at 1.5 to 2.5. When it passes into the duodenum, the acid from the stomach is neutralized by alkaline secretions from the pancreas, intestines and liver (12, 13).

The absorption of hydrochloric acid by the normal human stomach was studied by Shay et al. (14) after gastric intubation of fasted patients with 200 ml of a solution of approximately 0.5 percent (about 17 mg HCl per kg of body weight) or 1 percent (about 33 mg per kg) hydrochloric acid. Simultaneous intubation of olive oil into the duodenum arrested gastric evacuation. Thirty minutes after gastric administration, the stomach was emptied and the contents analyzed. It was found that the hydrochloric acid was not absorbed by the stomach under these conditions.

The introduction of hydrochloric acid into the stomach proportionately depresses the secretion of the acid by the stomach (15, 16). Thus when hydrochloric acid is ingested in small amounts, the total reaching the duodenum is little changed and is readily neutralized. When large quantities are consumed excess acid may escape neutralization and be absorbed, resulting in acidosis. Under acidic conditions, the normal bicarbonate-carbonic acid ratio of 27/1.35 in the plasma decreases and blood pH may fall to 7.0 or lower (16, 17). The decreased pH stimulates the respiratory center, and an increased depth and rate of respiration occur. This has the effect of lowering the carbonic acid concentration and restoring the pH to normal. In addition, the following renal compensatory mechanisms may develop: (a) an increased secretion and excretion of hydrogen ions; (b) stimulation of ammonium ion formation and excretion; (c) excretion of chloride ions with retention of bicarbonate; (d) slight decrease in sodium excretion because of the conservation and retention of bicarbonate, possibly resulting in a slight rise in the serum sodium concentration; (e) conversion of monohydrogen phosphate into dihydrogen phosphate and excretion of the latter (16, 17).

The addition of hydrochloric acid to test meals was reported to inhibit gastric motility and slow gastric emptying, this effect being mediated through duodenal receptors which are stimulated by the acid as it leaves the stomach (15, 18). The threshold for this effect was reported to be about 5 to 10 mN HCl, the effect increasing proportionally with increasing concentrations of acid (18). However, others have maintained that the acidity of the contents of the stomach and duodenum has no effect on the emptying time of the stomach (19-21).
Introduction of hydrochloric acid (0.1 N) into the stomachs of five or more anesthetized fasting dogs in each of 12 experiments was found by Code et al. (22) to inhibit gastric absorption of sodium but to have no effect on the absorption of water and potassium ion from the stomach.

Deloyers and Duprez (23) reported that hydrochloric acid produced a strong hypoglycemic effect when 250 ml of 0.6 percent acid (about 25 mg HCl per kg) was administered to 10 patients intraduodenally over a period of 20 minutes, the effect reaching its maximum in one hour after administration. However, Boattini (24) found that while hydrochloric acid exhibits a strong hypoglycemic effect on patients with diabetes mellitus, only a very slight effect is evident in normal subjects.

Acute toxicity

On the basis of reported cases of death from overdose with hydrochloric acid, Polson and Tattersall (25) suggested that the lethal dose of concentrated hydrochloric acid (38 percent hydrogen chloride) for man is probably 25 to 30 g or less.

Strong solutions of hydrochloric acid are highly corrosive. Because of immediate pain when taken into the mouth, the consumption of strong solutions of hydrochloric acid occurs only rarely (26). The immediate clinical manifestations are burning of the mouth and lips, frothing, and spitting, followed shortly by gagging and vomiting. Second-degree burns are occasionally produced in the esophagus, and stricture of the esophagus frequently develops (27-29). Tetanic contractions of the pylorus trap the acid in the stomach where perforation may occur and death ensue unless corrected surgically (26, 27, 30-32).

Strong solutions of hydrochloric acid do not occur in foods. The small amounts of the acid used in food preparation are neutralized by food constituents so that exposure of the consumer to any free acid seldom, if ever, occurs.

Short-term studies

In a 27-day feeding study using groups of 10 mixed-sex, one-day-old chicks, hydrochloric acid was added to the diet in concentrations of 0.21 (about 260 mg HCl per kg), and 0.42 percent (520 mg per kg). No significant effects were noted. However, a concentration of 0.84 percent (1 g per kg) in the diet resulted in a lower body weight gain and feed efficiency, but no mortality (33).

Burns (34) administered hydrochloric acid by gastric intubation to 16 rats for 9 weeks. The rats each received about 12 ml of 0.1 N acid
daily (about 100 mg HCl per kg) at the beginning of the experiment. This was gradually increased until at the end of 7 weeks each animal was receiving 50 ml of 0.1 N acid daily (about 500 mg per kg), and then for the last 2 weeks each animal received 50 ml of 0.2 N acid per day (about 900 mg per kg). After the dose of acid reached about 200 mg per kg the appetites of the animals decreased and the food supplied to the controls was adjusted to that of the experimental groups. After 9 weeks the treated rats died and the controls were sacrificed. Both bone and body growth were slightly retarded in animals consuming the acid, but there were no appreciable changes in the chemical composition of the bones. The base content of the soft tissues was increased slightly. Death was preceded by a marked loss in weight. Burns also administered hydrochloric acid to rabbits in doses of 45 ml (about 1.8 g per kg) to 200 ml daily (acid expressed in terms of N HCl) over 17 to 35 days. The animals receiving acid showed retarded growth or weight loss. Compared with litter mates on the same diet without acid, the treated rabbits showed a reduction in the base content of their muscles. There was a marked reduction in fat content of the bones, but no reduction in the percentage of ash.

Upon oral administration of 3.65 g of 0.1 N hydrochloric acid daily (about 10 mg HCl per kg) for 3 days to two human subjects, Stehle and McCarty (35) observed increased urinary excretion of potassium, sodium, ammonia, phosphoric acid and hydrogen ions.

The influence of acid-feeding on the utilization of mineral elements was examined by Telfer (17) through an experiment in which a 6-year-old child was fed exclusively for a period of 6 days, 1.8 l of milk per day which had an apparent hydrochloric acid concentration of 0.05 N (about 130 mg of HCl per kg body weight per day). The analysis of the excreta was compared with that of excreta over similar periods, before and after the experimental period, when no hydrochloric acid was added to the milk. An increase in the renal output of calcium, magnesium, and phosphorus was interpreted as indicating increased absorption of calcium, magnesium, and phosphorus. The quantities of these elements which were retained were slightly diminished. The author concluded from these results that hydrochloric acid adversely affects the process of calcification, presumably through the production of acidosis, and stated that earlier investigations had also shown that the administration of hydrochloric acid is followed by an increased urinary excretion of calcium and phosphorus.

**Long-term studies**

No reports of long-term studies were available to the Select Committee.
Carcinogenicity

Suntzeff et al. (36) injected 0.25 ml of 0.5 percent hydrochloric acid (about 60 mg per kg) subcutaneously into eight mice 6 times a week for 10.5 months. The acid was buffered to pH 5 with potassium acid phthalate. It was observed that spindle cell sarcomas developed at or near the site of injection in four of the eight mice but it was not determined whether it was the acid itself which induced the tumor or the 1.02 percent solution of potassium acid phthalate used to buffer the acid. Further, it was suggested that unidentified impurities in the phthalate solution may have been the real cause of the tumor formation.

Dyer et al. (37) gave hydrochloric acid orally to mice 5 to 10 times weekly for up to 11 months with (40 mice) or without (58 mice) 1, 2, 5, 6-dibenzanthracene. Acid doses ranged from about 90 to 360 mg HCl per kg. At necropsy some of the animals exhibited hemorrhage in the gastric mucosa, presumably as a result of the irritating effects of the acid. In no case did the treatment produce cancer. Only one mouse which had received 92 doses of hydrochloric acid and 11 doses of dibenzanthracene over a period of 8.5 months showed an inflammatory reaction about the base of the gastric glands, and some hyperplastic cells.

Teratogenicity

Landauer (38) injected about 1 mg of hydrogen chloride in 0.55 N solution into the yolks of White Leghorn eggs prior to incubation. After injection of the acid, 3.5 ± 0.6 percent of all embryos surviving the 17th day were rumpless, while among the controls (untreated eggs) the incidence of rumplessness was 1.9 ± 0.5 percent. In another experiment, in which 0.05 ml of concentrated hydrochloric acid (not otherwise specified) was injected, 3.8 ± 1.1 percent of the embryos were rumpless as against 0.8 ± 0.5 percent in untreated controls. No significant increase in the frequency of malformations other than rumplessness, i.e., lack of normal rump formation, was observed. In many of the embryos, some of the synsacrocaudal vertebrae were missing in addition to the free tail vertebrae. In certain of the extreme cases the posterior end of the body was edematous. Among the rumpless chicks which hatched there were some which had a partial tail skeleton. The authors concluded that while the concentrated hydrochloric acid probably produced some increase in the incidence of rumplessness, this was not true for more dilute hydrochloric acid.

Dostal (39) injected 17 mouse fetuses on the 13th day of gestation intraamniotically with 2 μl of 0.1 M hydrochloric acid (less than 0.01 mg); 41 fetuses serving as controls received physiological saline. At the time of examination on the 16th day of gestation no teratogenic effects were observed. Fetal mortality, however, was slightly (5.8 percent) increased by the acid injections.
V. OPINION

Hydrochloric acid in concentrated form is a strongly corrosive agent and the consequences of exposure to it are well-known. However, as it is used in food processing, or as a food additive to adjust the pH, hydrochloric acid is neutralized or buffered by the food to which it is added. Thus, human consumption is not of the acid, but of the chloride ion in the salts formed in the neutralization process. The small amounts of hydrochloric acid that may persist in foods or drinks, would, in turn, be neutralized and buffered during ingestion and digestion, or after absorption. Hydrochloric acid is also a natural secretory product of the stomach of animals, including man (about 0.5 percent concentration in the gastric juice). The normal production of hydrochloric acid by the stomach exceeds manyfold the amounts that could be derived from foods.

Animal experiments have not revealed untoward effects of hydrochloric acid consumption in amounts greatly exceeding those that can be reasonably expected to result from consumption of foods treated with hydrochloric acid.

Based on these considerations, the Select Committee concludes that:

There is no evidence in the available information on hydrochloric acid 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 the future.
VI. REFERENCES CITED


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Report submitted by:

July 30, 1979

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Select Committee on GRAS Substances