EVALUATION OF THE HEALTH ASPECTS OF CAPRYLIC ACID

AS A FOOD INGREDIENT

1974

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.

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

This report evaluates the health aspects of using caprylic acid 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 caprylic acid as a food ingredient. The Select Committee received no requests for such a hearing on caprylic acid.

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 substantive

*The document is available from the National Technical Information Service, U.S. Department of Commerce, P.O. Box 1553, Springfield, Virginia 22161.
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 caprylic 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

Caprylic acid is the common name for octanoic acid, \( \text{CH}_3(\text{CH}_2)_8\text{COOH} \), a saturated fatty acid. As an eight carbon compound it is among the fatty acids considered to be of short or medium chain length. It is a colorless, oily liquid having a mildly unpleasant odor and a burning, rancid taste (2). It is only slightly soluble in water (68 mg per 100 ml at 20\(^\circ\)) \( \text{C} \). It is a natural component of coconut and palm nut oils and butter fat. Caprylic acid has also been identified in trace amounts in beer (3,4), brandy distillate (5), the essential oil of fermented Russian black tea leaves (6), and raw soybeans (7).

The Food Chemicals Codex (2) specifications for caprylic acid include an acid value between 366 and 396, an iodine value of not more than 2.0, and the following limits of impurities: arsenic, not more than 3 ppm; heavy metals (as lead), not more than 10 ppm; unsaponifiable matter, not more than 0.2 percent.

Caprylic acid is listed as GRAS in 21 CFR 121.101(d)(2) as a chemical preservative in cheese wraps. It is regulated under 21 CFR 121.1070 (fatty acids) for use in foods as a lubricant, binder, or defoaming agent in accordance with good manufacturing practice, and as a component in the manufacture of other food grade additives. In addition, it is permitted as one of several aliphatic acids in lye peeling solutions (21 CFR 121.1091) and as a synthetic flavoring substance and adjuvant (21 CFR 121.1164). It is used in the artificial flavors of butter, coconut, pineapple, honey, brandy and cheese (8). Caprylic acid is used in the foods and in the
amounts shown in Table I (9). The Select Committee has no information concerning the extent to which the amounts of caprylic acid added to these foods may have changed in recent years.

Table I

<table>
<thead>
<tr>
<th>Food category</th>
<th>Caprylic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Usual</td>
</tr>
<tr>
<td></td>
<td>percent</td>
</tr>
<tr>
<td>Baked goods, baking mixes</td>
<td>0.0009</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>0.0004</td>
</tr>
<tr>
<td>Frozen dairy desserts, mixes</td>
<td>0.0001</td>
</tr>
<tr>
<td>Meat products</td>
<td>0.0004</td>
</tr>
<tr>
<td>Soft candy</td>
<td>0.0004</td>
</tr>
<tr>
<td>Gelatins, puddings, mixes</td>
<td>0.0005</td>
</tr>
<tr>
<td>Snack foods</td>
<td>0.0041</td>
</tr>
<tr>
<td>Beverages Type I (nonalcoholic)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Beverages Type II (alcoholic)</td>
<td>0.0003</td>
</tr>
<tr>
<td>Gravies, sauces</td>
<td>0.0002</td>
</tr>
<tr>
<td>Dairy products analogs</td>
<td>0.0004</td>
</tr>
<tr>
<td>Hard candy</td>
<td>0.0004</td>
</tr>
<tr>
<td>Chewing gum</td>
<td>&lt;0.0001</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 (see explanatory notes in exhibit 50 of reference 9).
III. CONSUMER EXPOSURE DATA

A National Research Council subcommittee (9) has provided information on the possible daily intake of caprylic acid added to foods as shown in Table II for individuals in various age groups. The Select Committee has converted these figures to possible intakes per kilogram of body weight.

Table II

Possible Daily Intake of Caprylic Acid

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total intake, mg</th>
<th>Intake, mg per kg body weight*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 mos.</td>
<td>0.05</td>
<td>0.01/0.03</td>
</tr>
<tr>
<td>6-11 mos.</td>
<td>0.44</td>
<td>0.06/0.15</td>
</tr>
<tr>
<td>12-23 mos.</td>
<td>0.82</td>
<td>0.07/0.20</td>
</tr>
<tr>
<td>2-65+ yrs.</td>
<td>2.00</td>
<td>0.03/0.09</td>
</tr>
</tbody>
</table>

*Calculations based on an average weight of 60 kg for an adult (10) and the following estimated weights of infants by age groups: 0-5 mos., 5 kg; 6-11 mos., 8 kg; 12-23 mos., 11 kg (11).

Inasmuch as the NRC subcommittee has recognized that its calculations of intakes in most cases are overstated, often by considerable margins,* the daily intakes indicated in Table II should be compared to the reported total use of caprylic acid in foods. From annual poundage data also included in the NRC subcommittee report (9) it can be calculated that 1,162 kg of caprylic acid were used in food in 1970. If one assumes a U.S. population of 210 million, this amount could supply less than 0.02 mg per person per day, an amount smaller than any of the estimated intakes in Table II.

*An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee's report (9). 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 of the intake of substances used in food processing, food consumption data collected specifically for this purpose are needed."
IV. BIOLOGICAL STUDIES

Caprylic acid occurs normally in various foods and is metabolized and utilized by the body as a non-essential fatty acid. It is absorbed in the gut and transported to the liver through the portal circulation as are other short chain fatty acids (12). For both the free acid (12) and its triglycerides (13), absorption is about 93 to 98 percent complete in rats. Similar data have been obtained in a case of pediatric chylothorax confirming the animal studies (14).

Feeding caprylic acid for 47 weeks to rats as part of a preparation consisting of medium-chain triglycerides (75 percent octanoic acid and 25 percent decanoic acid) resulted in decreased fat deposition and in little, if any, deposition of caprylic acid in depot fat (13). Most of the caprylic acid appears to be oxidized to acetate and acetyl coenzyme A in the liver and in the intestinal mucosa without prior esterification (12, 15, 16). A number of other investigators have reported results that are consistent with this metabolic pathway (17-20). Studies with isotope-labelled caprylic acid in vivo and in vitro suggest that the rate of oxidation to acetoacetate, acetyl coenzyme A, and carbon dioxide is very rapid (21-24). An alternative pathway, such as palmitate synthesis was observed for a limited amount of the acid (18, 23).

In human studies, 1.0 g per kg body weight of a mixture of medium-chain triglycerides containing 80 percent caprylic acid ingested by ten men and four women after an overnight fast, resulted in an elevation in blood serum ketone bodies and a fall in blood serum glucose (25). Using $^{13}$C-caprylic acid, oxidation of the acid was found to occur in two males and two females on thyroid substitution therapy (26).

The oral LD$_{50}$ for rats of mixed isomers of octanoic acid was reported as 1.41 ml per kg (estimated to be about 1.3 g) (27). The intravenous LD$_{50}$ of the glyceride tricaprylin for rats was found to be 3.7 g per kg (28). Intraperitoneal injection of sodium octanoate had a narcotic effect in rats but as much as 1 g per kg of body weight was without toxic effects (29). When young rats were fed a preparation consisting of medium-chain triglycerides (about 75 percent octanoic acid and 25 percent decanoic acid) as 19.6 percent of the diet for 47 weeks (more than 5 g of octanoic acid per kg body weight per day), no significant effects were observed on weight gain, or organ weight, or on histological examination of sections of liver and intestine (13). Fat deposition in the epididymal fat pad, liver, and carcass was reduced and a reduction in plasma cholesterol was noted in male rats. Rats were fed the same medium-chain triglyceride preparation at the 19.6 percent level for two generations and it caused no adverse effects on reproduction or abnormalities in any of the
fetuses. A reduction in milk secretion was noted in first generation
dams and was suggested by the authors as a factor in reduced weight
gain and relatively higher mortality in the second generation (13).

Feeding caprylic acid at a level of 5 percent in the diet (about
3.5 g per kg per day) resulted in serum cholesterol and triglyceride
levels that were somewhat lower than those produced by palmitic acid
but higher than those produced by stearic acid when fed in a hyper-
lipemic diet to 160 g male rats for 6 weeks (30). Feeding 8 percent
sodium caprylate (about 6 g per kg per day) in the diet of rapidly
growing male rats for up to 56 days did not affect their ability to utilize
dietary protein and energy sources efficiently (31).

The Select Committee has found no reports concerned with possible
mutagenic, teratogenic, or carcinogenic effects associated with the
feeding of caprylic acid.

V. OPINION

Caprylic acid, a naturally occurring constituent of many foods, is
absorbed and metabolized by man. Triglycerides containing this fatty
acid are hydrolyzed in the intestinal mucosa and the liberated fatty acids
are transported in the portal circulation and are almost completely
oxidized in the liver. Significant oxidation also appears to occur in the
intestinal mucosa. Little caprylic acid is stored, and long-term feeding
at high levels results in decreased overall fat storage that is indicative
of nutritional utilization. Thus caprylic acid is a fatty acid nutritionally
utilizable by man and animals.

Based upon consideration of the data presented in this report the
Select Committee concludes that:

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


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February 28, 1975
Date

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Select Committee on GRAS Substances