EVALUATION OF THE HEALTH ASPECTS OF GARLIC
AND OIL OF GARLIC AS FOOD INGREDIENTS

FEBRUARY 1973

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

(This document has not been approved for public release.)

Contract No. FDA 72-85
EVALUATION OF THE HEALTH ASPECTS OF GARLIC
AND OIL OF GARLIC AS FOOD INGREDIENTS

FEBRUARY 1973

Prepared for

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

(This document has not been approved for public release.)

Contract No. FDA 72-85

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) food substances that are being made by the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB) under contract with the Food and Drug Administration (FDA) of the U. S. Department of Health, Education, and Welfare. The Federation recognizes that the safety of GRAS substances is of national significance, and its resources are particularly suited to marshalling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office, established in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

Qualified scientists were selected as consultants to make a continuing review, analysis, and evaluation of the available information on each of the GRAS substances. These scientists, designated the Select Committee on GRAS Substances, were chosen for their competence and judgment with due consideration for balance and breadth in the appropriate professional disciplines. Members of the Select Committee on GRAS Substances who have contributed to this report are named in Section VII. The Select Committee's evaluations are being made independently of FDA or any other governmental or nongovernmental group.

These reports are approved by the Select Committee prior to submission to FDA. Although most LSRO consultants are members of FASEB constituent societies, the reports do not necessarily reflect the views of the Federation as a corporate body or carry the endorsement of the members of its constituent societies.

C. Jelkeff Carr
C. Jelkeff Carr, Ph. D., Director
Life Sciences Research Office
FASEB
<table>
<thead>
<tr>
<th>CONTENTS</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Introduction</td>
<td>1</td>
</tr>
<tr>
<td>II. Background information</td>
<td>2</td>
</tr>
<tr>
<td>III. Consumer exposure data</td>
<td>3</td>
</tr>
<tr>
<td>IV. Biological studies</td>
<td>5</td>
</tr>
<tr>
<td>V. Opinion</td>
<td>7</td>
</tr>
<tr>
<td>VI. References cited</td>
<td>8</td>
</tr>
<tr>
<td>VII. Scientists contributing to this report</td>
<td>12</td>
</tr>
</tbody>
</table>
I. INTRODUCTION

Under terms of FDA Contract 72-85, FASEB'S Life Sciences Research Office was requested to evaluate the health aspects of using garlic and oil of garlic as food ingredients, primarily on the basis of information contained in a monograph furnished by FDA (1), summarizing the world's scientific literature from 1920 through 1970, and in certain supplemental documents available as of February 1973. Garlic and oil of garlic are food substances that have been generally recognized as safe (GRAS) under the provisions of Section 121.101 of the Code of Federal Regulations (21 CFR 121.101, revised January 1, 1972).

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321(s)], GRAS substances are exempt from the requirement of premarketing clearance for food additives. It is stated in 21 CFR 121.1 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. It is recognized 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 accord 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, and realizes that a decision, based on such reasoned judgment, is expected even in instances where the available information is qualitatively or quantitatively limited. The Committee is also aware that biological testing, like all of science, is dynamic. Accordingly, the Committee's decisions, based as they are on the information now available, cannot anticipate and be guided by experiments not yet done or by the results of tests that may be reconduted, using new technologies that are constantly being evolved. These decisions 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 garlic and oil of garlic and submits its interpretation and assessment in this report, which is intended for the use of FDA in determining the future status of garlic and oil of garlic under the Federal Food, Drug, and Cosmetic Act.

II. BACKGROUND INFORMATION

Garlic is obtained from Allium sativum. In this genus of the lily family the underground bulb consists of a stem core surrounded by storage leaves rich in sugar and pungent allyl derivatives. The compound bulb is made up of several wedge-shaped bulblets, or "cloves." Other Allium species used for food beside garlic are onion, leeks, shallots and chives (1,2,3). Historical records reveal garlic has been used in foods dating back to 4500 B.C. (4).

In addition to the natural form, garlic is marketed as: (a) minced dehydrated garlic, (b) garlic powder, which is ground dehydrated cloves, (c) garlic salt, which is garlic powder mixed with table salt, and if necessary, some edible starch to prevent caking, and (d) oil of garlic, which is steam distilled from crushed garlic bulbs (1).

Major chemical constituents of whole garlic include alliin (allylsulfanyl alanine), which is rapidly converted enzymatically when garlic is crushed to allicin (allylsulfanyl allylsulfide), volatile and fatty acids, mucilage, and albumin. The principal compounds of garlic oil obtained by steam distillation of fresh garlic are disulfides, such as allylpropyl disulfide, diallyl disulfide, and diallyl trisulfide. Dimethyl sulfide, dimethyl disulfide, diallyl sulfide and dimethyl trisulfide have also been identified in the volatile fraction of the oil (1,5).

The Food Chemicals Codex specifications for food grade garlic oil establish ranges for the refractive index and specific gravity (6).

Besides its use as a flavoring in food, garlic has also been tried for medicinal purposes as a carminative (7), antihelminthic (8), antibacterial (9), and as a hypotensive agent (10).

In the food industry, garlic and garlic oil are used as flavoring in amounts ranging from 5,500 to 40 ppm (garlic) and from 34 to 1 ppm (garlic oil) in the following food categories, arranged in decreasing
order of content—garlic: gravies, processed vegetables, meat products, condiments and relishes (1,300 ppm), soups (40 to 800 ppm), and baked goods. Garlic oil: condiments and relishes, meat products, fats and oils, gravies (10-15 ppm), baked goods, snack foods (5-10 ppm), soft candy, nonalcoholic beverages, frozen dairy products and gelatin puddings (11).

There is no information available to the Select Committee to indicate whether the garlic or garlic oil content of the foregoing food categories has changed significantly in recent years.

III. CONSUMER EXPOSURE DATA

A comprehensive survey by a National Research Council subcommittee has provided information on the possible daily human intake of garlic oil in the total diet, as shown in the following table for individuals in various age groups (11). The Select Committee has converted these figures to possible intakes per kilogram of body weight.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Possible daily intake</th>
<th>Per kilogram of body weight*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Average</td>
</tr>
<tr>
<td></td>
<td>mg mg</td>
<td>mg</td>
</tr>
<tr>
<td>0-5 mos.</td>
<td>0.08 0.14</td>
<td>0.02</td>
</tr>
<tr>
<td>6-11 mos.</td>
<td>0.88 2.31</td>
<td>0.11</td>
</tr>
<tr>
<td>12-13 mos.</td>
<td>1.60 3.13</td>
<td>0.15</td>
</tr>
<tr>
<td>2-65+ yrs.</td>
<td>4.05 7.27</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*Calculations based on an average weight of 60 kg for an adult (12) and the following estimated weights of infants by age groups: 0-5 mos., 5 kg; 6-11 mos., 8 kg; and 12-23 mos., 11 kg. (13).
Other data in the NRC survey (11) indicate that 15,467 pounds of oil of garlic were reported by respondents to have been used in foods in 1970 and that this amount represented about 60 percent of the total amount used in U. S. foods. From these data it can be calculated that the total annual use of garlic oil in food is 25,778 pounds (11,717 kg). On the basis of this figure, only enough garlic oil is used by the food industry to provide for an average daily per capita consumption of 0.16 mg of garlic oil rather than the 4.05 mg indicated in the foregoing table. Accordingly, the Select Committee regards the figures in the table as overstatements of the possible daily per capita consumption of garlic oil in all age groups. This point has been recognized by the NRC subcommittee.*

Corresponding figures for the daily human intake of garlic itself cannot be drawn from the NRC data. However, an approximation of the average per capita daily intake of garlic can be derived from estimated domestic production and import data. The annual domestic production of garlic has averaged 53 million pounds over the past ten years (14) and the equivalent of some 20 million pounds of garlic is imported annually in the form of the fresh or dehydrated product (15). Thus, the average annual total that could be available for food use in the U. S. is about 73 million pounds (33 million kg). Assuming no wastage, this means that average per capita consumption in the U. S. could be approximately 452 mg of fresh garlic per day. Since distillation of fresh garlic is reported to yield 0.2 percent or less of garlic oil (2), this 452 mg of fresh garlic could contain about 1 mg of garlic oil.

On the basis of the foregoing, the Select Committee estimates that the average combined daily per capita intake of garlic oil, in the form of garlic and of the oil itself, is in the range 1 to 5 mg, with the likelihood that it is closer to the lower figure.

* An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee's report (11). 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."
IV. BIOLOGICAL STUDIES

Daily oral doses of a partially purified aqueous alcohol extract of garlic bulbs, equivalent to 40 g of garlic per kg had no effect on guinea pigs except for a slight loss of weight (16). In the case of rats, continuous daily ingestion of the same extract, equivalent to about 138 g of garlic per kg also resulted only in a slight loss of weight. The intravenous LD$_{50}$ of the extract for the rat and mouse was reported as the equivalent of 500 g of garlic per kg. It should be noted that the relationship between the composition of the alcohol extract used in the foregoing studies and garlic oil is not directly ascertainable from the data available. However, if one assumes that this investigator's alcohol extract contained all of the garlic oil present in the garlic bulbs extracted, a rough calculation can be made based on a content of 0.2 percent garlic oil in fresh garlic (2). On this basis the 40 g of garlic per kg indicated above would be equivalent to 80 mg of garlic oil per kg.

The subcutaneous LD$_{50}$ of allicin, one of the major constituents of oil of garlic, is reported to be 50 mg per kg in mice; the intraperitoneal LD$_{50}$, 20 mg per kg (17). According to Cavallito and collaborators (18, 19) extraction of fresh garlic yields 0.3 to 0.5 percent allicin. On the basis of 0.5 percent, the figures given above would be equivalent to about 10 g and 4 g of fresh garlic per kg, respectively.

The intraperitoneal LD$_{50}$ for mice of diallyl sulfide, one of the reported constituents of oil of garlic, is 500 mg per kg (20). The "qualifying toxic dose" for man by inhalation for another reported constituent of oil of garlic, allylpropyl disulfide, is a concentration of 3.4 ppm in air (20).

Six of ten guinea pigs on a 5 to 20 percent fresh garlic diet died within 28 days and all five rats died within 11 days on a diet of 20 to 30 percent fresh garlic (21). However, the addition of 3 percent garlic to the diet of young leghorn chicks, resulted in increased rate of growth (22).

There is no reported information on the absorption, metabolism or excretion of garlic, garlic oil, or their major constituents.

In an investigation of the effects of garlic powder in controlling infectious chronic lung congestion, it was noted that Wistar rats on a 2.5 percent dehydrated garlic diet, equivalent to 10 percent fresh garlic,
showed a slight lowering of the hemoglobin concentration and red cell count (23). On a diet of 5 percent dehydrated garlic, equivalent to 20 percent fresh garlic, the second generation rats were sterile.

A decrease in blood pressure was observed both in the first five minutes and in the following hour when rabbits were given 0.015 mg per kg of "garlic juice" (24). The pressure gradually returned to its original level after two hours. No side effects were noted.

When garlic juice, obtained by pressing, was administered orally to guinea pigs at a level of 1 cc per kg body weight daily, the blood calcium level increased to a peak between 14 and 28 days, but became normal again after 2 months of the same diet (25). A comparable reaction has also been reported in dogs (26).

No reports have been found that suggest garlic or garlic oil to be carcinogenic. On the other hand, antitumor potentialities have been claimed. For example, in one series of investigations, the feeding of fresh garlic was reported to completely prevent the development of mammary tumors in female mice, and the effect was attributed to the allicin component (27). It has also been reported that a 2 mg injection of a 1 percent ethyl alcohol extract of whole garlic altered the estrous cycle of ovariectomized rats (28). Crude garlic extracts, injected intraperitoneally, exerted an antimitotic effect similar to that of colchicine on the cells of ascites sarcoma in albino rats (29).

Investigations of the mutagenicity and teratogenicity of garlic or garlic oil have not been reported.

In addition to the foregoing limited toxicological data, two biological observations have been reported during the course of investigations of the medicinal properties of garlic and garlic oil. Ingestion by man of 10, 100 or 200, mg of garlic oil per day did not affect the blood erythrocyte count (30). Inhalation of garlic juice diluted in physiological salt solution or with 0.25 percent of a 1:3 procaine solution, by 34 patients with chronic pneumonia complicated by candidiasis of the lungs brought about an improvement in 26 of the patients (31). There was a decrease or disappearance of the candida fungus from the sputum of 16 patients.

Several reports have been made on allergic reactions to garlic, including asthmatic reaction to inhalation of garlic powder (32) and contact dermatitis (33). Food allergenic reactions with symptoms
similar to Meniere's disease have been reported for garlic (34) and
resemble those earlier found for certain foods, among them various
fruits, tomatoes, hazelnuts, potatoes, pork, lobster, eggs and other
foods (35). These studies of allergic reactions to garlic and foods
containing garlic were case reports; definitive investigations of aller-
genicity of garlic and its constituents are lacking.

V. OPINION

The long history of the use of garlic in food and acute, chronic and
inhalation studies, although limited, reveal no credible adverse biolog-
ical effects even at concentrations which are of orders of magnitude
greater than the levels reported to be currently consumed in man's
daily diet.

In view of the foregoing, the Select Committee concludes that:

There is no evidence in the available informa-
tion on garlic or oil of garlic that demonstrates
a hazard to the public when they are used at
levels that are now current or that might reason-
ably be expected in future.
VI. REFERENCES CITED


VII. SCIENTISTS CONTRIBUTING TO THIS REPORT

1. Members of the Select Committee on GRAS Substances:

Aaron M. Altschul, Ph.D., Professor, Department of Community Medicine and International Health, School of Medicine, Georgetown University, Washington, D. C.

Joseph F. Borzelleca, Ph.D., Professor of Pharmacology, Medical College of Virginia, Health Sciences Division, Virginia Commonwealth University, Richmond, Va.

Bert N. La Du, Jr., M.D., Ph.D., Professor and Chairman, Department of Pharmacology, New York University School of Medicine, New York, N. Y.

John R. McCoy, V.M.D., Professor of Comparative Pathology, New Jersey College of Medicine and Dentistry, Rutgers Medical School, New Brunswick, N. J.

Sanford A. Miller, Ph.D., Professor of Nutritional Biochemistry, Massachusetts Institute of Technology, Cambridge, Mass.

Gabriel L. Plaa, Ph.D., Professor and Chairman, Department of Pharmacology, University of Montreal Faculty of Medicine, Montreal, Canada.

Ralph G. H. Siu, Ph.D., Consultant, Washington, D. C.

John L. Wood, Ph.D., Distinguished Service Professor, Department of Biochemistry, University of Tennessee Medical Units, Memphis, Tenn.

George W. Irving, Jr., Ph.D. (Chairman), Research Associate, Life Sciences Research Office, Federation of American Societies for Experimental Biology, Bethesda, Md.
2. LSRO staff:

C. Jelleff Carr, Ph.D., Director, LSRO/FASEB.
Samuel B. Detwiler, Jr., Research Associate, LSRO/FASEB.
Kenneth D. Fisher, Research Associate, LSRO/FASEB.
Andrew F. Freeman, Research Associate, LSRO/FASEB.

3. Ad hoc consultant:

Henry Stevens, Ph.D. (USDA Retired), Consultant on Allergens,
Washington, D. C.

Report submitted by:

June 27, 1973
Date

George W. Irving, Jr., Chairman
Select Committee on GRAS Substances