EVALUATION OF THE HEALTH ASPECTS OF DILL

AS A FOOD INGREDIENT

MAY, 1973

Prepared for

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

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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) 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 experience 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. Jellett Carr
C. Jellett Carr, Ph.D., Director
Life Sciences Research Office
FASEB
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I. INTRODUCTION

Under terms of FDA Contract 72-85, FASEB's Life Sciences Research Office was requested to evaluate the health aspects of using dill as a food ingredient, 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 May, 1973. Dill is a food substance that has been generally recognized as safe (GRAS) under the provisions of Section 121.101 of the Code of Federal Regulations (21 CFR 121.101, revised April 1, 1973).

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321(s)], GRAS substances are exempt from the requirement of premarking 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 conclusion 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 conclusions, 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 reconducted, using new technologies that are continually being evolved. 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 dill and submits its interpretation and assessment in this report, which is intended for the use of FDA in determining the future status of dill under the Federal Food, Drug, and Cosmetic Act.

II. BACKGROUND INFORMATION

Dill is an herb which has been used for its presumed medicinal properties and its flavoring characteristics since early Anglo-Saxon times. Dill oil is the essential oil obtained by steam distillation of the freshly cut stalks, leaves, and seeds (dill herb or dill weed oil, American), of the crushed, dried fruit or seeds (dill seed oil, European), or of the crushed mature fruit of Indian dill (dill seed oil, Indian). Yield of oil varies up to about 4 percent depending on the nature and condition of the source material. The first two (American and European) are produced from *Anethum graveolens*, L., the last (Indian) from *Anethum sowa*, D. C. (1,2,3). European dill is produced principally in England, Germany and Hungary; Indian oil in India and Japan.

Commercial production of dill in the United States, largely in Ohio, Idaho, and Oregon, was started in 1930 although it was grown as a garden plant prior to that time. Present commercial production is sufficient to make the United States independent of foreign sources for dill herb oil, the product preferred by the American food industry. However, appreciable quantities of European and Indian seed oils are imported (2).

Dill herb and seed oils are reported to contain carvone, d-limonene and phellandrene as major constituents and lesser or trace amounts of terpinene, myristicin, isomyrysticin, dipentene, dihydrocarvone, α-pinen, caryophyllene, eugenol, anethole, anisaldehyde, thymol and two coumarin derivatives, scopecotin and 6,7-dihydro-8,8-dimethyl-2H,8H-benzo(1,2-b:5,4-b') dipyran-2,6-dione (2, 4, 5, 6). Dillapiol and probably its isomer, apiol, have been reported to occur in Indian dill (*A. sowa*) but not in American and European dill (*A. graveolens*) (7). Recent chromatographic analyses of several samples of undistilled dill of known origin confirm the absence of dillapiol in *A. graveolens* (8).

Percentage figures for the content of the several constituents in
the distilled oil of dill plants or seeds have little significance, since the relative amounts of the components are not constant; shifts occur at least in the content of carvone, limonene, and phellandrene, depending on the state of maturity of the plant and seed (2, 7). For example, the carvone content increases in the plant from before flowering to fruit ripening while limonene, which is apparently a precursor of carvone, decreases as the fruit matures (2).

Structures of some of the major reported constituents of dill oils are provided on the following page to show interrelationships. Isomers of most of these components quite likely occur during the development of the plant, and hence, may occur in the distilled oils.

It is to be noted that myristicin and the apiolanes are closely related; all three can be considered to be methoxy derivatives of safrole. However the Select Committee has found no reports of the presence of safrole in dill or dill products.

The three general types of dill oils differ somewhat in flavor, odor, and composition depending on source, season of harvest, and processing procedures. The Food Chemicals Codex distinguishes between the food grade products largely on the basis of their content of one of the major constituents, carvone (9). The specifications for identity and purity provide that:

American dill weed oil should usually assay not less than 28 percent and not more than 45 percent by volume of ketones as carvone, although early season oil may show a carvone content as low as 25 percent;

European dill seed oil should assay not less than 42 percent and not more than 60 percent ketones as carvone; and

Indian dill seed oil should assay not less than 20 percent and not more than 30 percent of ketones as carvone.

The specifications also recognize differences in specific gravity, optical rotation, and refractive index, and set limits for content of arsenic, heavy metals and lead (9).

The GRAS list (10) includes "dill (Anethum graveolens, L.)" under
both the spices and the essential oils, oleoresins and natural
extractives, but it does not specifically include the products of
*Aethrum soua*, D. C. It includes also the following reported con-
stituents of dill oil: d- or l-carvone; d-, l-, and dl-limonene;
eugenol; and anethole. Listed as GRAS under another section of
the Code of Federal Regulations (11) are dihydrocarvone, \( \alpha \)-phell-
landrene, \( \alpha \)-pinene, \( \alpha \)-and \( \gamma \)-terpinene, \( \beta \)-caryophyllene, and
thymol. This section also includes isoeugenol and several deri-
vatives of both eugenol and isoeugenol. The GRAS list of the
Flavor Extract Manufacturers' Association (12) includes dill, dill
oil, Indian dill seed, carvone, d-limonene, \( \alpha \)-phellandrene,
eugenol, \( \alpha \)-pinene, \( \beta \)-caryophyllene, anethole, thymol and dihydro-
coumarin; coumarin is not so included.

Dill seeds or the powdered herb are used for flavoring
foods but dill oil, because of its greater uniformity, is more
frequently used in the food industry, usually in the form of dill
water, a solution of dill oil in aqueous alcohol (2).

Dill, dill oil, and Indian dill seed are used as flavoring
agents in the following categories of foods arranged approximately
in decreasing order of content (13): **Dill** (5950 to 275 ppm) in cheese,
gravies and sauces, baked goods, condiments and relishes, meat
products, processed vegetables, and fats and oils; **dill oil** (750 to
<1 ppm) in snack foods, condiments and relishes, cheese, gravies
and sauces, alcoholic beverages, meat products, fats and oils,
baked goods, gelatins, puddings and fillings, soft candy, frozen
dairy desserts, nonalcoholic beverages, hard candy and chewing
gum; **dill seed, Indian** (29,000 to 410 ppm) in condiments and
relishes, baked goods, meat products, and fats and oils.

A National Research Council subcommittee survey (13)
indicates that 88,365 pounds (40,166 kg) of dill, 106,300 pounds
(48,318 kg) of dill oil and 316,972 pounds (144,078 kg) of Indian
dill seed were used in food in the United States in 1970. These
amounts represent about 60 percent of the actual amounts used.
Import statistics for 1968 through 1972 (14) indicate that total
annual imports of dill have tended to increase slightly in recent years,
amounting to about 885,000 pounds (402,222 kg) in 1971, of which more
than 90 percent came from India. The Census of Agriculture (15)
reports that 3,009 acres of dill were grown commercially in 1969
but no data are available to indicate how much of the crop was
marketed and used as seed, seed oil, or herb oil. However,
most of the domestic dill is presumably processed to herb oil,
the product preferred by the American food industry. Based on a
yield of 30 pounds of herb oil per acre (2) annual domestic production, if all had been used for this purpose, could have been of the order of 90,000 pounds (41,000 kg) of the oil in 1969. None of these data provide the Select Committee with information to indicate the extent to which total poundage used or the dill content of the foregoing food categories may have changed in recent years.

III. CONSUMER EXPOSURE DATA

The survey by the National Research Council subcommittee (13) has provided information on the possible daily intake of dill products in the total diet, as shown in the following table for individuals in various age groups. The Select Committee has converted these figures to possible intake per kilogram of body weight.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Possible daily intake</th>
<th>Per kilogram of body weight</th>
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<tbody>
<tr>
<td></td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dill : Dillseed : Indian : Dill : Dillseed : Indian</td>
<td></td>
</tr>
<tr>
<td></td>
<td>oil : seed : oil : seed</td>
<td></td>
</tr>
<tr>
<td>Av 'Max'</td>
<td>Av 'Max'</td>
<td>Av 'Max'</td>
</tr>
<tr>
<td>mg' mg:</td>
<td>mg' mg:</td>
<td>mg' mg:</td>
</tr>
<tr>
<td>0-5 mos.:</td>
<td>12' 17:</td>
<td>0.4' 0.8:</td>
</tr>
<tr>
<td>6-11 mos.:</td>
<td>101'216:</td>
<td>4.8'13.5:</td>
</tr>
<tr>
<td>12-23 mos.</td>
<td>211'360:</td>
<td>10.3'24.1:</td>
</tr>
<tr>
<td>2-65+ yrs.:</td>
<td>520'802:24.1</td>
<td>51.9:</td>
</tr>
</tbody>
</table>

1 Calculations based on an average weight of 60 kg for an adult (16) 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 (17).

The figures in the foregoing table must be considered in respect to the domestic production, importation and use of dill in foods. The NRC subcommittee has pointed out that its calculations of intakes in most cases are overstated, often by considerable margins. 2 That this is true in the case of dill is borne out by the

2 An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee's report (13). 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."
following calculation: Other NRC data show that in 1970 the use for food purposes in the U. S. was 88,365 pounds (40,166 kg) of dill, 106,300 pounds (48,318 kg) of dill oil, and 316,972 pounds (144,078 kg) of Indian dill seed. It is stated that these reported figures comprise between 60 and 70 percent of the total actual poundage used in foods. On the basis of 60 percent adjusted to 100 percent and a U. S. population of 200 million, the per capita per day average intake would be 0.9 mg of dill, 1.1 mg of dill oil, and 3.3 mg of Indian dill seed, rather than the 520, 24, and 654 mg, respectively, indicated in the table.

Rough estimates of possible intakes can also be made based on total imports and domestic production of dill. In 1971, 885,000 pounds (402,222 kg) of dill were imported (14). This 402,222 kg would provide for an average per capita daily intake of about 5.5 mg of dill. Domestically produced dill in 1969 would yield (see Section II of this report) some 90,000 pounds (41,000 kg) of dill oil, if all were to be processed to dill oil, providing enough for an average per capita daily intake of about 0.56 mg of dill oil.

In the light of these considerations, the Select Committee regards the figures given in the foregoing table as levels that are highly unlikely to be achieved by any of the age groups, but are more likely to be generous overestimates of the dill content of the human diet. A daily per capita average intake of dill, equivalent to about 1 mg of dill oil (0.017 mg per kg per day for adults) appears to be a more reasonable overall estimate. The NRC subcommittee (13) indicates that children of ages 6-23 months consume up to 2.5 times as much dill per kg of body weight as do adults.

The Joint FAO/WHO Expert Committee on Food Additives (18) has established a conditional acceptable human daily intake up to 1.25 mg per kg body weight of the sum of 1- and d-carvone, the principal constituents of dill oil. The term "conditional" means that the substance may be employed within the specified limits with an adequate margin of safety if it has been reviewed by experts for the particular use. For comparison, the carvone equivalent of the 1 mg per capita per day average intake of dill oil arrived at as indicated above, can be estimated on the basis that the oil contains a maximum of 60 percent carvone. Thus the daily per capita carvone equivalent in the diet would be no more than 0.6 mg, a figure comparable to that established as acceptable by FAO/WHO.
IV. BIOLOGICAL STUDIES

There is a paucity of information on the biological effects of dill or the essential oils derived from the plant or seed.

Dill oil derived from A. graveolens, as well as the essential oils from a number of other spices, exhibit an antispasmodic and myotropic effect on rabbit and guinea pig intestinal strips in vitro (19). Dill has been used historically as an aromatic carminative (20). It is reported to induce rebuilding of damaged tissues in hemorrhoidal cases (21).

Some toxicity data are available on the principal constituents of dill oil. The oral LD₅₀ of carvone in the rat is reported as 1640 mg per kg (22). The following oral LD₅₀'s in mg per kg also are reported (23): eugenol, 500 in the rat; myristicin, 570 in the cat; anethole, 2090 in the rat; anisaldehyde, 1510 in the rat; thymol, 1000 in the mouse. Oral LD₅₀'s for eugenol ranging from 1930 to 2680 mg per kg in the fasted rat have also been reported (24, 25, 26).

Pure carvone was found to have no adverse effect on 5 male and 5 female rats fed 2500 ppm in the diet (approximately 250 mg per kg per day) for 1 year (27); but at 10,000 ppm for 16 weeks, growth retardation and testicular atrophy were observed. Eugenol, thymol, or anisaldehyde, fed at a level of 10,000 ppm in the diet for 15 to 19 weeks, had no effect. Anethole, fed at 2500 ppm for a year, produced no effect; but at 10,000 ppm for 15 weeks it produced slight microscopic hydropic changes of hepatic cells in males.

As noted previously, dillapiole, and probably its isomer apirole, are present in significant but variable amounts in the oil of Indian dill (A. sowa) but occur only in trace amounts, if at all, in the oil from A. graveolens. Since about half of the dill consumed in U. S. foods is estimated to be of Indian origin, the available biological information on dillapiole and its relatives is important in consideration of dill.

Apirole, an isomer of dillapiole from parsley, is reported to have been used as an abortifacient and as such produced polyneuritis in a number of cases in Holland; but, this effect was shown to be due to a contaminant, tri-o-cresol phosphate (28, 29). An apirole of 96 percent purity was lethal to dogs when fed at a level of 0.5 to 0.75 g per kg (30). Rabbits fed doses of 2.25 to 20 g of apirole for 6 days to 2 months developed lesions of the liver and kidneys (31). An oral LD₅₀ of 1 to 1.5 g per kg is reported
for dillapiole in mice (32). The same investigators observed no toxic effects of A. graveolens oil containing no dillapiole or of A. sowa oil containing dillapiole, or effects on blood pressure or heart rate (32). After ingestion of 1.6 g of apirole for 3 days, 2 individuals excreted the compound in the urine on the first day and one on the second and third days. There was no detectable apirole in the blood (33).

No reports are available to the Select Committee that bear on the possible carcinogenic, mutagenic, reproductive or teratogenic effects of feeding dill or oil of dill, or their major constituents.

V. OPINION

The Select Committee estimates that daily consumption of dill probably does not exceed the equivalent of 1 mg of dill oil per capita, or about 0.017 mg per kg per day in adults and about twice that level in children. The oil's most plentiful constituent, carvone, present to the extent of about 60 percent in the oil, elicits toxic responses only at levels much greater than those that might be present in the diet. Other constituents, present in some oils in lesser to trace amounts, such as apirole, dillapiole, and myristicin have not been shown to produce toxic effects on feeding at levels many times those that could exist in man's diet.

The Select Committee has weighed the foregoing and concludes that:

There is no evidence in the available information on dill and dill oils that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current or that might reasonably be expected in future.
VI. REFERENCES CITED


substances and non-nutritive sweetening agents. 11th rept. Food and Agriculture Organization of the United Nations, Rome, Italy.


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.

Harry G. Day, Sc.D., Professor of Chemistry, Indiana University, Bloomington, Ind.

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, Ph.D., Research Associate, LSRO/FASEB.
Andrew F. Freeman, Research Associate, LSRO/FASEB.

Report submitted by:

October 12, 1973

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