EVALUATION OF THE HEALTH ASPECTS OF METHYLPOPSILICONES AS FOOD INGREDIENTS

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

Contract No. FDA 223-78-2100
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Life Sciences Research Office
Federation of American Societies for Experimental Biology
9650 Rockville Pike
Bethesda, Maryland 20014
NOTICE

This report, one of a series concerning the health aspects of using the Generally Recognized as Safe (GRAS) or prior-sanctioned food substances as food ingredients, is being made by the Federation of American Societies for Experimental Biology (FASEB) under Contract No. 223-78-2100 with the Food and Drug Administration (FDA), U.S. Department of Health and Human Services. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshaling 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 Dockets Management Branch, 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.

Kenneth D. Fisher, Ph.D., Director
Life Sciences Research Office
FASEB
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I. INTRODUCTION

This report concerns the health aspects of using methylpolysilicones as food ingredients. It has been based partly on
the information contained in a scientific literature review (monograph) furnished by FDA (Dailey, 1978), which summarizes the world's
scientific literature from 1920 through 1978. To ensure 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; searches for relevant data in the
files of FDA; and by the combined knowledge and experience of mem-
bers of the Select Committee and the LSRO staff. In addition, an
announcement was made in the Federal Register of November 7, 1980
(45 FR 74056-74060) that opportunity would be provided for any
interested person to appear before the Select Committee at a pub-
lic hearing to make oral presentation of data, information, and
views on the health aspects of using methylpolysilicones as food
ingredients. The Select Committee received no requests for such a
hearing.

As indicated in the Food, Drug, and Cosmetic Act [21 USC
321(s)], GRAS substances are exempt from the premarketing clear-
ance that is required for food additives. It is stated in the Act
and in the Code of Federal Regulations (Office of the Federal Reg-
ister, 1980) [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 sec-
tions of the Code also indicate that expert judgment is to be
based on the evaluation of results of credible toxicological test-
ing 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 pat-
terns of consumption, cumulative effects in the diet, and safety
factors appropriate for the utilization of animal experimentation
data. FDA recognizes further [21 CFR 170.30] that it is impos-
sible to provide assurance that any substance is absolutely safe
for human consumption.

The Select Committee on GRAS Substances of LSRO reviewed
and evaluated the available information on methylpolysilicones in
full recognition of the foregoing provisions. In reaching its con-
clusions on safety, the Committee, in accordance with FDA's guide-
lines, relied primarily on the absence of substantive evidence of,
or reasonable grounds to suspect, a significant risk to the public
health. This report is intended for the use of FDA in determining
the future status of these substances under the Federal Food, Drug,
and Cosmetic Act. The Committee anticipates that its conclusions
will be reviewed as new information becomes available.
II. BACKGROUND INFORMATION

Methylpolysilicones (also called dimethylpolysiloxanes) are high-molecular weight organic compounds of silicon which are similar in chemical structure to inorganic silicates. They are members of a large family in which silicon and oxygen atoms form a siloxyl skeleton to which various alkyl and aryl groups are attached in regular, repetitive fashion. The methylpolysilicones may be characterized by the following formula:

![Methylpolysilicone Structure](image)

where "n" can be varied from 0 to 10,000 or higher.

The commercial methylpolysilicones are usually linear polymers, although cyclic forms may also be utilized (The Condensed Chemical Dictionary, 1977). This report is limited to methylpolysilicones and will not consider the numerous commercial silicones produced with other alkyl or aryl groups which may alter profoundly the biological properties of the silicone (Palazzolo et al., 1972).

Methylpolysilicones can be prepared in viscosity grades ranging from one to several hundred thousand centistokes (cs) depending on the degree of polymerization. Those employed in food uses generally have "n" values of 200–400, with molecular weights usually between 14,000 and 21,000 (The United States Dispensatory, 1973). In this molecular weight range, methylpolysilicones are clear, colorless, viscous liquids, which may contain up to 5% silicon dioxide. With higher degrees of polymerization, resins and rubbers are produced. The methylpolysilicones are insoluble in water and the lower alcohols, but soluble in most aliphatic and aromatic hydrocarbon solvents. The polymers are nonionic, inert compounds strongly resistant to chemical and thermal attack. They are hydrophobic, greasy, and markedly antiadhesive.

Commercial methylpolysilicone preparations frequently contain silica gel as well as emulsifying agents and preservatives (Joint FAO/WHO Expert Committee on Food Additives, 1970). Food-grade methylpolysilicones must meet the following specifications (National Research Council, 1972):

- Refractive index: 1.400 to 1.404
- Specific gravity: 0.964 to 0.973
- Viscosity: 300 to 600 cs
- Loss on heating: not more than 18%
- Limit of impurities: arsenic, not more than 3 parts per million (ppm); heavy metals, not more than 10 ppm (expressed as lead)
The antifoaming and hydrophobic properties of dimethylpolysilicones are also utilized medically in patients suffering from excessive gas production or retention such as flatulence, gastric bloating, or postoperative gaseous distention. They have also been used to reduce gas shadows in radiography of the bowel and to improve visualization in gastroscopy (Swinyard, 1975). The usual therapeutic adult dose is 150-400 mg daily (National Formulary, 1975). Silicones are also employed to prevent dermal irritation in bedridden patients (Bateman, 1956; Carter and Sherman, 1957). Medical grade preparations (simethicone) must contain 93–99% dimethylpolysilicone, not more than 4.5% silicon dioxide, and have a viscosity not less than 300 cs (National Formulary, 1975).

Because of their chemical and thermal resistance together with their antiadhesive and hydrophobic properties, methylpolysilicones have found various uses in the food industry. They are used to coat containers and molds for bakery products, candies, and confections; to impregnate packaging and wrapping paper which contact foods; and to reduce foaming in various fermentation and canning processes (Anonymous, 1970; Sluzewska, 1970). Methylpolysilicones at low concentrations (0.03-0.05 ppm) reduce thermal and oxidative deterioration of frying fat by forming a protective film at the oil-air interface. At higher levels (1-10 ppm), silicones added to shortening and other frying fats may eliminate smoking difficulties by raising the smoke point 20–30°F (Sims and Stahl, 1970). Silicones have also been incorporated into cellulosic sausage casings to facilitate the casing removal from the enclosed meat mass (Chiu and Veith, 1967).

Food grade methylpolysilicones are marketed by several American manufacturers (Dow Corning, General Electric, SWS-Silicone, Union Carbide) but published data appear confined to Dow Corning preparations, especially Antifoam A®, which is representative of this group (Chinn, 1980). Antifoam A® has a bimodal molecular weight distribution with the major peak at 19,000 and a minor peak at 290. Although regulations permit up to 18% of low molecular weight polymers, Antifoam A® generally contains about 10% and consists predominantly of tetramers, pentamers, and hexamers (LeVier et al., 1977).

The authorized uses of methylpolysilicones in foods, food packaging, and food contact surfaces are listed are listed in Table 1. This report considers the prior-sanctioned uses.
### Table 1. Authorized Uses of Methylpolysilicone in Foods, Food Packaging, or Food Contact Surfaces

<table>
<thead>
<tr>
<th>Function</th>
<th>Component of</th>
<th>Authorization</th>
<th>Identity or limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior-Sanctioned</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Release agent</td>
<td></td>
<td>21 CFR 181.28 (Office of the Federal Register, 1980)</td>
<td>Substantially free from hydrolyzable chloride and alkoxy groups. Not more than 18% loss in weight after heating 4 hours at 200°C; viscosity 300-600 cs at 25°C; specific gravity 0.96-0.97 at 25°C. Refractive index 1.400-1.404 at 25°C</td>
</tr>
<tr>
<td>Not specified</td>
<td>Not specified</td>
<td>Letter (Cassidy, 1960)</td>
<td></td>
</tr>
<tr>
<td>Release agent</td>
<td>Maple syrup bottles</td>
<td>Letter (Cassidy, 1961)</td>
<td>Less than 10 ppm in food</td>
</tr>
<tr>
<td>Antifoaming agent</td>
<td>Gelatin dessert products</td>
<td>Letter (Kleber, 1963)</td>
<td>Not to exceed 10 ppm</td>
</tr>
<tr>
<td>Other Authorized Uses</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Defoaming agent</td>
<td></td>
<td>21 CFR 173.340</td>
<td>Same as for 21 CFR 181.28, Also: 10 ppm in food or at such level in a concentrated food that, when prepared as directed on the labels, the food in its ready-to-eat state will not have more than 10 ppm, except as follows: zero in milk; 110 ppm in dry gelatin dessert mixes labeled for use whereby no more than 16 ppm is present in the ready-to-serve dessert; 250 ppm in salt labeled for cooking purposes, whereby no more than 10 ppm is present in the cooked food</td>
</tr>
<tr>
<td>Not specified</td>
<td>Adhesives</td>
<td>21 CFR 175.105</td>
<td></td>
</tr>
<tr>
<td>Function</td>
<td>Component of</td>
<td>Authorization</td>
<td>Identity or Limitations</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------------------------------------</td>
<td>------------------------</td>
<td>----------------------------------------------</td>
</tr>
<tr>
<td>Other Authorized Uses (cont'd)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Release agent</td>
<td>Resinous and polymeric coatings</td>
<td>21 CFR 175.300</td>
<td>Curling catalyst must contain not more than 1 part tin per 100 parts of siloxane resin</td>
</tr>
<tr>
<td>Release agent</td>
<td>Xylene-formaldehyde resin as food contact surfaces</td>
<td>21 CFR 175.380</td>
<td></td>
</tr>
<tr>
<td>Release agent</td>
<td>Zinc-silicon dioxide matrix coatings as food contact surfaces</td>
<td>21 CFR 175.390</td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>Paper and paperboard that contact with aqueous and fatty foods</td>
<td>21 CFR 176.170</td>
<td>100 cs viscosity</td>
</tr>
<tr>
<td>Not specified</td>
<td>Paper and paperboard that contact with dry food</td>
<td>21 CFR 176.180</td>
<td>100 cs viscosity</td>
</tr>
<tr>
<td>Defoaming agent</td>
<td>Coatings</td>
<td>21 CFR 176.200</td>
<td></td>
</tr>
<tr>
<td>Defoaming agent</td>
<td>Paper and paperboard materials</td>
<td>21 CFR 176.210</td>
<td></td>
</tr>
<tr>
<td>Defoaming agent</td>
<td>Cellophane</td>
<td>21 CFR 177.1200</td>
<td></td>
</tr>
<tr>
<td>Release agent</td>
<td>Closures with sealing gaskets on containers contacting food</td>
<td>21 CFR 177.1210</td>
<td></td>
</tr>
<tr>
<td>Release agent</td>
<td>Ethyl vinyl acetate copolymers contacting food</td>
<td>21 CFR 177.1350</td>
<td></td>
</tr>
<tr>
<td>Elastomer</td>
<td>Ethylene polymer, chlorosulfonated</td>
<td>21 CFR 177.2210</td>
<td></td>
</tr>
<tr>
<td>Fiber finishing agent</td>
<td>Resin-bonded filters used repeatedly</td>
<td>21 CFR 177.2260</td>
<td></td>
</tr>
<tr>
<td>Elastomer</td>
<td>Rubber articles intended for repeated use</td>
<td>21 CFR 177.2600</td>
<td></td>
</tr>
<tr>
<td>Function</td>
<td>Component of</td>
<td>Authorization</td>
<td>Identity or Limitations</td>
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<tr>
<td>----------------</td>
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<td>----------------------------------</td>
</tr>
<tr>
<td><strong>Other Authorized Uses (cont'd)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not specified</td>
<td>Textiles and textile fibers</td>
<td>21 CFR 177.2800</td>
<td>(Office of the Federal Register, 1980)</td>
</tr>
<tr>
<td>Lubricant</td>
<td>Lubricant with incidental food contact</td>
<td>21 CFR 178.3570</td>
<td>Viscosity greater than 100 cs. Addition to food not to exceed 1 ppm</td>
</tr>
<tr>
<td>Lubricant</td>
<td>Surface lubricants used in manufacture of metallic articles</td>
<td>21 CFR 178.3910</td>
<td>Conforms to identity described in 21 CFR 181.28</td>
</tr>
</tbody>
</table>
III. CONSUMER EXPOSURE

The level of addition of methylpolysilicone to foods by food category is shown in Table 2. The total quantity used in foods, as reported to the Committee on GRAS List Survey—Phase III (1978), declined by almost 50% during the period 1970–1975 (Table 3), to a per capita daily intake in 1975 of about 8 μg.

The Codex Alimentarius Commission (1969a,b; 1970) has temporarily endorsed a level of 10 mg/kg of dimethylsilicone singly or in combination with silicon dioxide as the maximum level of use in edible fats and oils, safflower oil, and mustardseed oil.

Sluzewska (1970) undertook a preliminary evaluation of silicone which might migrate from packaging materials to foods. Silicone-coated paper, produced in Poland from a methylsilicone resin emulsion, was cut into small circles and extracted at room temperature for 24 h with distilled water, 3% acetic acid, or heptane to simulate neutral, acid, or fat-containing foods. The mean values of the dry residues extracted (in excess of noncoated paper controls) were 0.15, 0.10, and 0.42%, respectively.
Table 2. Level of Addition of Methylpolysilicones to Foods by Food Category*

<table>
<thead>
<tr>
<th>Food Category</th>
<th>Number of firms reporting</th>
<th>Methylpolysilicone weighted mean mg/kg</th>
<th>Technical effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fats and oils</td>
<td>6</td>
<td>8.7</td>
<td>Surfactant</td>
</tr>
<tr>
<td>Processed fruits, juices, and drinks</td>
<td>&lt;4</td>
<td>5.0</td>
<td>Surfactant</td>
</tr>
<tr>
<td>Condiments, relishes, salt substitutes</td>
<td>&lt;4</td>
<td>33.0†</td>
<td>Antifoam</td>
</tr>
</tbody>
</table>

* Subcommittee on Review of the GRAS List--Phase II (1972).
† Volunteered information.

Table 3. Consumption of Methylpolysilicones Based on Total Quantity Used Annually in Foods

<table>
<thead>
<tr>
<th>Substance</th>
<th>Relative amounts used* 1975:1970</th>
<th>Total used, kg† 1970 1975</th>
<th>Per capita daily intake, mg§ 1975</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylpolysilicones</td>
<td>0.51</td>
<td>1310 659</td>
<td>0.008</td>
</tr>
</tbody>
</table>

* Based on data from respondents to both 1970 and 1975 National Research Council Surveys (Committee on GRAS List Survey--Phase III, 1978).
† Seven companies reported in 1970, six companies in 1975.
§ Based on total use in 1975 and a U.S. population of 215 million.
IV. BIOLOGICAL STUDIES

Absorption, distribution, metabolism

The wide range of molecular weights and viscosities, as well as the profusion of cryptic proprietary names of the methylpolysilicones, make it difficult to compare the various reports on the biological activity of this group of polymers. An attempt has been made to confine discussion to those preparations which meet food grade specifications, although this was not always possible.

Methylpolysilicones are poorly absorbed from the gastrointestinal tract. Virtually none of the high molecular weight polymers and only small amounts of the lower polymers (usually tetrarimer, pentamers, or hexamers) are absorbed. Investigators at the University of Birmingham (1967a,b; 1968) could detect no significant absorption of Antifoam M® when fed to rats, rabbits, dogs, or human subjects for periods of 4 to 120 d. This is a medical grade preparation consisting of 6% finely divided silicon dioxide and 94% methylpolysilicone with a viscosity of 350 cs. The methylpolysilicone has a mean molecular weight of 22,000 with less than 0.2% low molecular weight polymers (LeVier et al., 1977). Monkeys (Anonymous, 1974) were given oral doses of 21.8 or 41.8 mg/kg body wt of 14C-labeled methylpolysilicone essentially free of low molecular weight species. Recovery in the feces amounted to 93-97% of the administered dose, with 0.001-0.22% found in the urine, and 0.01-0.02% in the expired air. Forty tissues from one animal were analyzed 72 h after administration. The total cumulative radiolabel in these tissues was less than 0.01% of the administered dose (Anonymous, 1974). Similarly, no silicone was detected in the tissues of male or female mice receiving 2.5% in their diet (about 3 g/kg/d) for 76 wk (University of Birmingham, 1970).

Antifoam M® was given by mouth to six human subjects in single doses in sesame oil (100 mg/kg body wt) (Anonymous, 1974; LeVier et al., 1977). No increase of urinary silicon was detected and no organosilicon compounds were detected in the exhaled air of the individuals. Subjects receiving the same amount of Antifoam A® (viscosity 350 cs), however, excreted 1.8-3.3% of the administered dose in the urine as silicon or as an unidentified organosilicon compound. About 0.35% of the administered Antifoam A® was exhaled in the expired air. As noted earlier, significant amounts of low molecular weight polymers are present in Antifoam A®, whereas Antifoam M® contains very little of these compounds.

Little, if any, silicone is metabolized in the body to carbon dioxide. Monkeys given 14C-labeled methylpolysilicone (viscosity not stated) by mouth, excreted only traces in their expired air (Anonymous, 1974). No radioactivity could be detected in the expired air of rats injected intramuscularly with 14C-labeled silicone DC200® (viscosity 350 cs) (McGregor, 1960).
Acute toxicity

Rowe et al. (1948) administered DC200® by stomach tube to guinea pigs. The dose employed in the acute test was so large that it could not be given at one time. Therefore, 5 ml were given every half-hour until the required volume was reached. The guinea pigs received a total of 5-50 ml (about 7-70 g/kg body wt). None died within the 7-d observation period. The only response appeared to be a laxative effect, which was most marked about 24 h after administration.

Reed and Kittle (1959) injected 0.2-1.2 g/kg of Antifoam A® intravenously into 31 mongrel dogs weighing from 8-13 kg. Sixteen animals died within 10 min of the injection, one after only 0.3 g/kg. The intravenous LD$_{50}$ was approximately 0.9-1.0 g/kg. Eight of 27 dogs died within 10 min when the preparation was administered intraarterially, one from a dose of 0.01 g/kg. The intraarterial LD$_{50}$ was 0.02 g/kg. Areas of infarction were noted in the brains. Some animals survived with signs of neurologic damage, chiefly hemiplegia.

Intradermal and subcutaneous injections of DC200® into rabbits caused no apparent effect beyond transitory minor trauma at the site of injection (Rowe et al., 1948). Application to shaved areas of rabbit skin produced no significant irritation. Instillation into rabbit or human eyes caused conjunctival irritation and edema of the lids, which disappeared after 24 h. No corneal damage was evident.

Short term studies

Rats

Rowe et al. (1948) fed DC200® methylpolisilicone by stomach tube repeatedly to young adult female rats derived from the Wistar strain. Twenty doses at levels of 1.0, 2.0, 5.0, 10.0, and 20.0 g/kg body wt in 4 ml of olive oil were given over 28 d to each of five animals per dosage level. A similar control group received 4 ml olive oil/animal/dose. The experimental animals, even at the highest dosage level, grew as well as the controls. Blood values of animals receiving 2 and 10 g/kg of the methylpolysilicone were not significantly different from those of control animals. Organ weights and bone marrow cell counts were normal. No histopathological changes of the heart, spleen, kidneys, liver, adrenals, pancreas, bone marrow, stomach, or intestine could be detected.

Methylpolysilicone fluids with viscosities of 50, 350, 1000, 10,000, and 60,000 cs were fed for 90 d at a dietary level of 1% (about 1 g/kg body wt/d) to 10 male and 10 female Holtzman rats (MacDonald et al., 1960). Nearly all experimental rats
gained less than the controls, but the differences in weight were not statistically significant. No pathological changes were noted except for pneumonitis and consolidation with the formation of caseous abscesses in the lungs of many of the animals of all groups, including controls. The authors attributed these changes to infection not related to the silicone ingestion. Leucocyte counts and hemoglobin levels were normal. No significant changes were seen on histological examination of the heart, liver, spleen, kidney, testis, ovary, aorta, uterus, stomach, or small or large intestine.

Pollard (1960) fed DC151® to two groups of rats (sex and strain not stated) for 15 wk at levels of 0.3 and 1.0% of their diet (about 300 and 1000 mg/kg body wt/d). DC151® was a silicone material under investigation for treatment of gastric, duodenal, and intestinal ulcers. The composition and viscosity were not reported. All of the rats "appeared to be in excellent condition" at the end of the experiment, with no hematological abnormalities.

Hobbs et al. (1972) utilized the atrophy of the rat seminal vesicle as a rapid assay to measure the toxicity of several methylpolysilicones. Of the silicones tested, DC200® was the only one whose viscosity met food grade specifications. Each of 10 adult male rats of FDLR strain received a daily oral dose of 3.3 ml (about 1.2 g/kg body wt) for seven consecutive days. The animals were fasted 24 h prior to the first dose and again 24 h prior to sacrifice. At necropsy, the final body weight and the weight of the seminal vesicles were determined. The animals receiving DC200® fluid did not differ significantly from controls in weight gain, behavioral response, testicular weights, or spermatogenic ability.

Carson et al. (1966) fed groups of five male and five female rats for 1 yr on diets containing 1% DC360® (viscosity 350 cs). The daily intake of each silicone was about 1 g/kg. No significant differences from controls were noted in weight gains, hematological indices, blood chemistries, urinalyses, organ weights, or histopathological examinations.

Frodsham (1956) maintained groups of five male and five female rats approximately 260 d on diets containing 0.0, 0.5, and 2% of a silicone emulsion consisting of 50% Antifoam A® with 2% pentaerythritol as an emulsifying agent (about 250 and 1000 mg silicone per kg body wt). No significant changes were noted in body or organ weights or in hematologic indices.

Investigators at the University of Birmingham (1967a) studied the toxicity of a silicone preparation consisting of 5% finely divided silicon dioxide and 95% methylpolysilicone oil (Antifoam Compound P9816, viscosity not stated). Ten male and ten female rats, 4 wk of age, from a randomly bred stock colony, were fed diets containing 0.1 or 1.0% of the silicone for 90 d. The authors estimated that the rats consuming the 1% silicone diet
received about 725 mg/kg body wt/d. There were no significant differences from controls in the animals of both groups in weight gains, hematologic indices, blood chemistries, urinalyses, or kidney or liver function tests. There were no pathological changes which could be attributed to the diet. No silicone could be detected in any of the tissues examined (spleen, kidney, liver, testes, intestine) nor any increase in urinary silicate excretion. The authors concluded that no, or only traces of, silicone was absorbed.

Cutting (1952) also fed six adult rats a diet containing 2% of either DC200® or Antifoam A® (about 2 g/kg/d) for 4 mo. No gross or microscopic abnormalities were observed in any of the organs examined.

Rabbits

Cutting (1952) fed male and female rabbits for 3 or 4 mo a diet containing 0.8% cholesterol to which DC200® or DC Antifoam A® silicone had been added in concentrations up to 1% (about 300 mg/kg/d). Of the ten rabbits given cholesterol and DC200® silicone, nearly all had differing degrees of kidney lesions. The kidneys showed moderately prominent white, linear streaks in the medulla, parallel with the tubules. The proximal convoluted tubules were distended with a clear material which did not stain with hematoxylin and eosin or with Sudan IV, and contained casts and protein. Some of the tubular epithelial cells showed foamy cytoplasm and others a brown pigment. The livers appeared normal on gross inspection, but revealed microscopically centrolobular hepatocytes with vacuolated cytoplasm. Some parenchymal cells contained intracytoplasmic clefts which had the shape of crystals.

Twelve rabbits given cholesterol and Antifoam A® in the doses indicated above, also showed kidney lesions, similar to those described above (Cutting, 1952). The liver showed some fat in the cytoplasm of hepatocytes in the periphery of the lobules and a considerable deposit of a clear material in the cells around the central veins. Similar clear intracytoplasmic deposits were seen in the cells of a grossly visible capsular thickening of the spleen and in masses of epithelial cells in the middle ear. The author speculated that the clear material seen in these specimens might be silicone, but no identification was attempted. Cholesterol alone did not produce any of the observed changes. The effect of the silicone alone was not studied.

Carson et al. (1966) repeated and extended Cutting's studies. He maintained rats for 1 yr and rabbits for 8 mo on diets containing 1% DC360® or 1% Antifoam A® alone or combined with 0.8% cholesterol. The daily intake of the silicone was estimated to be about 300 mg/kg body wt. No significant differences between control animals and those receiving the methylpolysilicones alone were detected in growth, hematologic indices, blood or urine analyses, organ weights, or tissue morphology. The
cholesterol-fed animals, however, both with and without the methyl-
polysilicone, showed widespread cellular infiltration by clear
material. The investigators concluded that cholesterol, rather
than silicone, was the prime causative factor of the observed
lesions in their study, and presumably in Cutting's study as well.

**Dogs**

Child et al. (1951) studied the short-term effects of
Antifoam A® in a group of mongrel dogs. The silicone had a grease-
like consistency comparable with white petrolatum. Two dogs at
each dose level were given 0.0, 0.3, 1.0, or 3.0 g/kg of the prep-
paration 5 d weekly. The dogs accepted the treated food without
hesitation. At the end of 6 mo, the organs and tissues of the
animals were examined grossly and microscopically. No significant
changes were found in the heart, lungs, spleen, pancreas, kidneys,
urinary bladder, striated muscle, gonads, stomach, small and large
intestine, adrenals, thyroid glands, or bone marrow. The liver of
each of the animals which had been fed the silicone had deposits
which were identified as bile pigment; quantities deposited in the
Kupffer and hepatic cells varied directly with the doses of the
silicone ingestion. Fine, discrete granules were seen in the
hepatic parenchymal cells. In dogs fed the highest dosage of the
methylpolysilicone, the pigment was also found in the interlobular
bile ducts.

For 8 mo, one adult male dog was fed 1.0 and a second dog
3.3 g DC151® silicone/kg body wt daily in divided doses. Body
weights were maintained and all blood and urine analyses were with-
in the normal range. Monthly biopsies of liver, spleen, kidneys,
and bone marrow revealed no significant changes (Pollard, 1960).

Antifoam M® was fed to 8-mo-old beagle dogs for 120 d
(University of Birmingham, 1968). The silicone was given to two
males and two females at levels of 300 mg/kg/d, with two dogs of
each sex serving as controls. The behavior and appearance of the
experimental animals remained normal. There was no effect on
weight gain, renal or liver function, blood cell composition,
hemoglobin, or serum electrolytes. The spleen of one female
showed areas of atrophy with fibrous trabeculation. One of the
male dogs showed fibrosis on the anterior wall of the greater cur-
vature of the stomach, which proved on necropsy to be a healed
ulcer. No trace of silicone was detected in tissues. The fecal
silicone output was approximately equal to the amount ingested.
The urinary silicates did not increase. The authors concluded
that Antifoam M® was not absorbed by dogs.

**Monkeys**

Two monkeys were fed 100 g and two others 300 g DC151®
5 d weekly for 8 mo (about 20 and 60 g/kg/d). One monkey receiv-
ing the larger dose vomited consistently during the first month.
Occasional diarrhea, exhibited by all monkeys, was the only other untoward effect reported (Pollard, 1960).

Fish

Bluegills and rainbow trout were exposed for 4 d to concentrations up to 10,000 ppm of DC Antifoam C® emulsion (30% emulsion of Antifoam A® compound). No deaths were noted at any level of the silicone exposure (Hobbs et al., 1975).

Other

Various salt water species, including cockles, mummichogs, crabs, and shrimp were exposed for 4 d to concentrations of 1-1000 ppm Dow Corning Antifoam C® emulsions. The median tolerance limit (4 d TL50) for all species was greater than 1000 ppm (Hobbs et al., 1975).

Man

The Joint FAO/WHO Expert Committee on Food Additives (1975) listed a number of investigations on the use of methylpolysilicones therapeutically in man at doses up to 200 mg/d with no apparent adverse effects. Pollard (1960) reported a study in which 27 patients were given 48 ml of DC151® (about 650 mg/kg) in divided doses for 3-13 mo (average 8 mo) without significant toxic effects except for occasional nausea. The frequency of administration was not stated. The Committee concluded that the acceptable daily intake of silicone by man was as much as 1.5 mg/kg body wt.

Long-term studies

Rowe et al. (1950) fed groups of 25 male and 25 female rats a modified Sherman diet containing 0.3% of Antifoam A® (about 300 mg/kg/d). After 2 yr on this diet, the average body weight of the male rats receiving the silicone was well above that of the controls. The female rats showed no difference in weight gains between test and control groups. There was no significant difference in organ weights (heart, liver, kidneys, spleen, and testes), blood urea nitrogen, or liver lipid between control and experimental groups. No histological changes were found which could be attributed to the prolonged silicone ingestion. In two or three animals of each group (including controls) hyaline casts were observed in the renal tubules, but in most cases the affected portions were not extensive. At necropsy most of the females showed various degrees of ovarian or uterine abnormalities, but these were considered to be common signs of senility.
Cutler et al. (1974) fed 40-50 each of male and female mice a diet containing 0.25 or 2.5% of Antifoam A® for 76 wk. The animals ingested an estimated 580 and 5800 mg silicone/kg/d, respectively. Five female and five male mice receiving the higher level of silicone for 75 wk were transferred to a control diet 8 d before sacrifice. No silicone was detected in whole body analyses of these animals. Similarly, no silicone was detected in samples of liver, kidneys, spleen, or perirenal fat from five mice given single subcutaneous injections of 0.2 ml silicone 76 wk previously. The only pathologic finding differing from control animals was an increased incidence of superficial gastric ulcers in the males receiving 0.25% silicone (but not in those receiving 2.5%), and a reduced incidence of uterine atrophy in the females fed the 2.5% silicone diet.

The Joint FAO/WHO Expert Committee on Food Additives (1975) cited an unpublished report by Frazer (1959) in which three groups of 30 female and 10 male rats were fed a diet containing 0.0, 0.01, or 0.1% silicone fluid (not further identified) for 2 yr. No significant differences from controls were detected. Growth, tumor incidence, liver function tests, urinalyses, fat absorption, renal function tests, and hematologic indices did not differ significantly from controls. No silicone was found in the gut wall, nor was there any significant increase in other organs. Two further generations were reared on the same diet. The F₁ generation was necropsied after 28 wk and the F₂ generation, after 25 wk.

The Joint FAO/WHO Expert Committee on Food Additives (1975) concluded that a level of 150 mg/kg/d in the rat caused no toxicological effects.

Carcinogenicity

Cutler et al. (1974), in the long-term study with Antifoam A® already discussed, found no increase above controls in the number of malignant or benign tumors in mice receiving silicone in their diet or by subcutaneous injection.

Reproductive and teratogenic effects

The Select Committee is not aware of any studies on the reproductive or teratogenic effects of methylpolysilicone administered by mouth. Kennedy et al. (1976) investigated the effects in rats and rabbits of subcutaneous injection of 20, 200, or 1000 mg DC360®/kg body wt. They concluded that the silicone was devoid of adverse effects on reproduction and fetal development in both species at these dose levels.
Mutagenicity

The Select Committee is not aware of mutagenicity studies employing silicones within the viscosity range utilized for food purposes.

Special studies

Nosanchuk (1968) investigated the antibody and histologic response of guinea pigs to DC360®. Six animals were injected initially in each heel pad with 0.5 ml of 1:1 mixture of Freund's adjuvant and the silicone. At weekly intervals (for 3 wk), 0.05 ml of the mixture was injected into each heel pad and 1.0 ml subcutaneously in the flank. Two additional four-dose courses of weekly flank injections were administered of 3:1 silicone-Freund's adjuvant mixture. Preinoculation and serial postinoculation sera were assayed for antibodies by passive cutaneous anaphylaxis, Ouchterlony gel diffusion, and immediate and delayed cutaneous hypersensitivity tests. In none was antibody production demonstrated.
V. OPINION

The methylpolysilicones used in food have been demonstrated to be of low acute and chronic toxicity to animals and man when administered orally. The present daily intake is about 0.1 μg/kg/body wt and their use in food appears to be decreasing.

No carcinogenic effects have been reported after oral administration. The Select Committee is not aware of reproductive or teratologic studies with silicones given by mouth. However, repeated subcutaneous injections into male and female rats and rabbits caused no significant adverse effects on reproduction or fetal development.

The bulk of the food grade methylpolysilicones consists of high molecular weight compounds which are not absorbed to any appreciable extent from the intestinal tract. However, these silicones may also contain some low molecular weight (<1000) polymers which might be absorbed. Prudence dictates that food grade specifications should be modified to minimize the presence of absorbable components.

The Select Committee concludes that:

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


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