EVALUATION OF THE HEALTH ASPECTS OF GELATIN

AS A FOOD INGREDIENT

1975

Prepared for

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

Contract No. FDA 223-75-2004
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Life Sciences Research Office
Federation of American Societies
for Experimental Biology
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. 223-75-2004 with the Food and Drug Administration (FDA), U.S. Department of Health, Education, and Welfare. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshalling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office (LSRO), established by FASEB in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

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

Tentative reports are made available to the public for review in the Office of the Hearing Clerk, Food and Drug Administration, after announcement in the Federal Register, and opportunity is provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the substances covered by the report. The data, information, and views presented at the hearing are considered by the Select Committee in reaching its final conclusions. Reports are approved by the Select Committee and the Director of LSRO, and subsequently reviewed and approved by the LSRO Advisory Committee (which consists of representatives of each constituent society of FASEB) under authority delegated by the Executive Committee of the Federation Board. Upon completion of these review procedures the reports are approved and transmitted to FDA by the Executive Director of FASEB.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of all of the individual members of its constituent societies.

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 gelatin 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 March 24, 1975 (40 FR 13016 and 13017) 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 gelatin as a food ingredient. The Select Committee received no requests for such a hearing on gelatin.

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 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

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

Gelatin does not occur in nature as such, but is derived by hydrolysis of collagen, the chief protein component in connective tissues of the animal body. Extraction of gelatin for use as a glue by cooking hides dates back to the earliest recorded history of man and appears in the literature of the times up to the present day. During the early years of the Napoleonic era it was manufactured on a large scale in an attempt to alleviate the food shortages resulting from the English naval blockade of Europe. Gelatin was first manufactured in the U.S. in 1809 (2). In 1845 a U.S. patent was granted for a gelatin which contained all the ingredients fitting it for table use, and required only the addition of hot water and subsequent cooling to prepare it for serving (3).

Quantitatively, collagen is concentrated in the skin, the bone of the skeletal system and the tendons attaching muscles to the skeleton, although it occurs throughout all of the tissues and organs to a lesser degree. Chemically, collagen and gelatin are virtually indistinguishable, but the process of collagen extraction results in converting the fibrous, water-insoluble, highly organized, macromolecules (tropocollagens) irreversibly into gelatin which has dissimilar physical characteristics. Variations in gelatin properties due to source and treatment make it a highly diverse, heterogeneous substance, particularly with regard to molecular weight (3).

The major sources of collagen are cattle hides, pig skins and bones. The resulting gelatin is of two types commonly designated A and B, depending upon which of two processes are used to convert the collagen into gelatin. Type A gelatin is derived primarily from pig skin by acid processing; Type B from cattle hides and bones by alkaline or lime processing. Gelatin from different sources and as prepared by the different processes exhibits small differences in amino acid composition as shown in Table I (3). The nutritionally essential amino acid, tryptophan, is absent in gelatin. Gelatin also is unusual in that it contains large proportions of glycine, proline and hydroxyproline, and a small percentage of hydroxylysine, amino acid rare in proteins.
<table>
<thead>
<tr>
<th>Amino acid</th>
<th>Type A percent</th>
<th>Type B (skin) percent</th>
<th>Type B (bone) percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine</td>
<td>8.6 - 10.7</td>
<td>9.3 - 11.0</td>
<td>11.3</td>
</tr>
<tr>
<td>Arginine</td>
<td>8.3 - 9.1</td>
<td>8.55 - 8.8</td>
<td>9.0</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>6.2 - 6.7</td>
<td>6.6 - 6.9</td>
<td>6.7</td>
</tr>
<tr>
<td>Cystine</td>
<td>0.1</td>
<td>None - Trace</td>
<td>Trace</td>
</tr>
<tr>
<td>Glycine</td>
<td>26.4 - 30.5</td>
<td>26.9 - 27.5</td>
<td>27.2</td>
</tr>
<tr>
<td>Glutamic acid</td>
<td>11.3 - 11.7</td>
<td>11.1 - 11.4</td>
<td>11.6</td>
</tr>
<tr>
<td>Histidine</td>
<td>0.85 - 1.0</td>
<td>0.74 - 0.78</td>
<td>0.70</td>
</tr>
<tr>
<td>Hydroxylysine</td>
<td>1.04</td>
<td>0.91 - 1.2</td>
<td>0.76</td>
</tr>
<tr>
<td>Hydroxyproline</td>
<td>13.5</td>
<td>14.0 - 14.5</td>
<td>13.3</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>1.36</td>
<td>1.7 - 1.8</td>
<td>1.54</td>
</tr>
<tr>
<td>Leucine</td>
<td>3.1 - 3.34</td>
<td>3.1 - 3.4</td>
<td>3.45</td>
</tr>
<tr>
<td>Lysine</td>
<td>4.1 - 5.2</td>
<td>4.5 - 4.6</td>
<td>4.36</td>
</tr>
<tr>
<td>Methionine</td>
<td>0.80 - 0.92</td>
<td>0.80 - 0.90</td>
<td>0.63</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>2.1 - 2.56</td>
<td>2.2 - 2.5</td>
<td>2.49</td>
</tr>
<tr>
<td>Proline</td>
<td>16.2 - 18.0</td>
<td>14.8 - 16.35</td>
<td>15.5</td>
</tr>
<tr>
<td>Serine</td>
<td>2.9 - 4.13</td>
<td>3.2 - 4.2</td>
<td>3.73</td>
</tr>
<tr>
<td>Threonine</td>
<td>2.2</td>
<td>2.2</td>
<td>2.36</td>
</tr>
<tr>
<td>Tyrosine</td>
<td>0.44 - 0.91</td>
<td>0.2 - 1.0</td>
<td>0.23</td>
</tr>
<tr>
<td>Valine</td>
<td>2.5 - 2.8</td>
<td>2.6 - 3.4</td>
<td>2.77</td>
</tr>
</tbody>
</table>

Food Chemicals Codex (4) does not list compositional standards for food-grade gelatin. The U.S. Pharmacopeia (5) provides standards for the product for pharmaceutical use which Glicksman (3) states most food gelatins meet. Ash, U.S.P. limit, 2 percent, is principally calcium phosphate in bone gelatin whereas that of Type A or pig skin gelatin is mainly sodium chloride and sulfate (3). U.S.P. limit for arsenic is 0.8 ppm and for heavy metals is 50 ppm. Standards for microbiological quality for food grade gelatin have been issued by FDA (6). These require an aerobic plate count (geometric mean) not greater than 3,000 per g and a coliform count (geometric mean) not greater than 10 per g.

The major use of gelatin in the U.S. is in food products, principally in gelatin desserts, meat products, consommés, marshmallows, candies, bakery and dairy products and ice cream. In 1972, 34.5 million pounds were produced in the U.S. for these uses (7) and an additional 9.7 million pounds of edible gelatin were imported (8). In 1961, the last year for which figures for consumption in food, pharmaceutical and industrial uses are available, 71 percent (41.2 million pounds) of domestic production went into food; 7.4 percent was used by the pharmaceutical industry; the remainder went mainly into photographic products (17.3 percent) with lesser amounts (4.4 percent or 2.55 million pounds) for other industrial uses including paper and textiles (9).
Gelatin is generally recognized as safe (GRAS) as a food ingredient (10) and also as a substance migrating to food from cotton fabrics used in dry food packaging (11). Table II, taken from the report of a survey made of the food industry by a subcommittee of the National Research Council (12) lists the food categories in which gelatin is used and also gives a weighted mean of the usual percentages reported by manufacturers who added gelatin to at least one food in the category. Each usage level reported by a manufacturer was multiplied by the ratio of total pounds used by that manufacturer in all food categories to the total pounds reported by all manufacturers in all food categories. Weighted mean values also were calculated for maximum levels of addition; these are not reported here.

No information has been found concerning the quantity of gelatin that is used in cotton fabrics for dry food packaging or concerning the amounts that might enter food products through migration or abrasion from such packaging materials.

III. CONSUMER EXPOSURE DATA

The National Research Council subcommittee (12) has estimated a possible daily human intake of gelatin by food category for various age groups (Table III). The Select Committee has converted the intake figures into possible intakes per kilogram body weight. Gelatin intake figures in Table III are not additive across food categories for the reasons given in the table footnote. The NRC subcommittee estimates were based on data from the Market Research Corporation of America on the frequency of eating foods from a given food category, USDA data on mean portion size for the various age groups and the assumption that all food products within a category contained gelatin at the level of addition given in Table II irrespective of manufacturer or specific food product. Such an assumption is likely to lead to an overestimate of the consumption of gelatin. The NRC subcommittee has pointed out that its calculations of intake are overstated in most cases, often by considerable margins.* Although not strictly comparable with the figures in Table III, a per capita daily intake of 262 mg for gelatin can be calculated from 1972 production and imports of edible

*An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee's report (12). 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."
TABLE II

Level of Addition of Gelatin to Foods by Food Category (12)*

<table>
<thead>
<tr>
<th>Food category</th>
<th>Weighted mean percent**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baked goods, baking mixes</td>
<td>1.75</td>
</tr>
<tr>
<td>Breakfast cereals</td>
<td>0.01</td>
</tr>
<tr>
<td>Grain products such as pastas or rice dishes</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Milk, milk products</td>
<td>0.42</td>
</tr>
<tr>
<td>Cheese</td>
<td>0.50</td>
</tr>
<tr>
<td>Frozen dairy desserts, mixes</td>
<td>0.29</td>
</tr>
<tr>
<td>Processed fruits, juices, drinks</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Meat products</td>
<td>1.18</td>
</tr>
<tr>
<td>Poultry products</td>
<td>1.00</td>
</tr>
<tr>
<td>Processed vegetables, juices</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sugar, confections</td>
<td>1.40</td>
</tr>
<tr>
<td>Sweet sauces, toppings, syrups</td>
<td>0.75</td>
</tr>
<tr>
<td>Gelatins, puddings, fillings</td>
<td>1.50</td>
</tr>
<tr>
<td>Soup, soup mixes</td>
<td>1.50</td>
</tr>
<tr>
<td>Snack foods</td>
<td>0.50</td>
</tr>
<tr>
<td>Beverages, alcoholic</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Gravies, sauces</td>
<td>2.00</td>
</tr>
<tr>
<td>Dairy products analogs</td>
<td>0.40</td>
</tr>
</tbody>
</table>

*Information on food uses of gelatin was not requested in the NRC subcommittee survey but was volunteered by respondents to the survey.

**For discussion of weighted mean see text, also Section X and Exhibit 50 of reference 12.
<table>
<thead>
<tr>
<th>Food category</th>
<th>0-5 months</th>
<th>6-11 months</th>
<th>12-23 months</th>
<th>2-65+ years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mg</td>
<td>mg/kg</td>
<td>mg</td>
<td>mg/kg</td>
</tr>
<tr>
<td>Baked goods, baking mixes</td>
<td>271</td>
<td>54</td>
<td>502</td>
<td>63</td>
</tr>
<tr>
<td>Breakfast cereals</td>
<td>1</td>
<td>&lt;1</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Grain products such as pastas or</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>rice dishes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk, milk products,</td>
<td>218</td>
<td>44</td>
<td>548</td>
<td>68</td>
</tr>
<tr>
<td>miscellaneous products</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheese</td>
<td>4</td>
<td>1</td>
<td>43</td>
<td>5</td>
</tr>
<tr>
<td>Frozen dairy desserts, mixes</td>
<td>20</td>
<td>4</td>
<td>44</td>
<td>5</td>
</tr>
<tr>
<td>Processed fruits,</td>
<td>1</td>
<td>&lt;1</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>juices, drinks</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meat products</td>
<td>128</td>
<td>26</td>
<td>354</td>
<td>44</td>
</tr>
<tr>
<td>Poultry products</td>
<td>100</td>
<td>20</td>
<td>109</td>
<td>14</td>
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<tr>
<td>Processed vegetables, juices</td>
<td>&lt;1</td>
<td>&lt;1</td>
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<td>&lt;1</td>
</tr>
<tr>
<td>Sugar, confections</td>
<td>3</td>
<td>1</td>
<td>11</td>
<td>1</td>
</tr>
<tr>
<td>Sweet sauces, toppings, syrups</td>
<td>62</td>
<td>12</td>
<td>19</td>
<td>2</td>
</tr>
<tr>
<td>Gelatins, puddings, fillings</td>
<td>352</td>
<td>70</td>
<td>344</td>
<td>43</td>
</tr>
<tr>
<td>Soups, soup mixes</td>
<td>63</td>
<td>13</td>
<td>724</td>
<td>90</td>
</tr>
<tr>
<td>Snack foods</td>
<td>2</td>
<td>&lt;1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Beverages, alcoholic</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Gravies, sauces</td>
<td>22</td>
<td>4</td>
<td>62</td>
<td>8</td>
</tr>
<tr>
<td>Dairy products analogs</td>
<td>&lt;1</td>
<td>&lt;1</td>
<td>66</td>
<td>8</td>
</tr>
</tbody>
</table>

*The figures in this table apply only to individuals who ate foods in the particular food category one or more times during the 14-day survey period, not to figures based on the amounts of food consumed by the entire survey population. The figures are valid for any particular substance on an individual food category basis only. They are not cumulative across all food categories, since no person could be expected to eat foods from all categories in any single day at the consumption levels shown.

*bCalculated intake, mg/kg body weight, based on an average weight of 60 kg for an adult (13) and the following estimated weights of infants by age groups: 0-5 mo, 5 kg; 6-11 mo, 8 kg; and 12-23 mo, 11 kg (14).
gelatin (44.2 million pounds) given earlier. The Select Committee regards the figures in Table III for most categories as levels that are unlikely to be achieved by any of the age groups.

IV. BIOLOGICAL STUDIES

Absorption, metabolism, excretion

Nixon and Mawer (15) reported the results of experiments in which six human volunteers were fed test meals containing milk protein or gelatin as the protein source. Intestinal contents were collected at various levels along the tract to study the distribution of the peptides and amino acids. Free amino acid concentrations in small intestinal contents in collections made 3 hours after ingestion were lower for the gelatin test meal as compared to the milk-protein meal. For both meals arginine, lysine, tyrosine, valine, phenylalanine, methionine and leucine appeared to be absorbed as the free amino acid. Glycine, threonine, serine, the imino acids, and dicarboxylic amino acids were released from the peptide form at very slow rates in the intestinal lumen and were not indicated to be absorbed as the free amino acids.

Mason and Palmer (16) determined the absorption and retention of gelatin in studies on the relative nutritional values of gelatin, casein and zein in the maintenance of adult rats. After feeding a nitrogen-free diet, 0.4 g (1 g per kg body weight) of each of the three proteins was added to the daily ration. Feces and urine were collected and analyzed for excreted nitrogen. Additional test protein was added to the diet in quantities required for nitrogen balance. After several days the animals were returned to the nitrogen-free diet and the excreted nitrogen was again determined. Zein was irregularly or poorly digested. Digestion and absorption of gelatin was complete, although it was poorly utilized and had a retention of only 23 percent as compared to casein, 74 percent, and zein, 57 percent.

That storage of creatinine and creatine might occur after ingestion and absorption of gelatin was indicated to Dill and Horvath (17) who studied four human subjects given 60 g of gelatin daily for a 40-50 day period as supplements to their usual diets. They noted that creatine excretion increased in two subjects but the average creatinine excretion was not changed. Creatine and creatinine excretion did increase after the diet period was terminated, suggesting storage. Hueckel and Rogers (18) fed diets containing gelatin, free amino acids or their mixtures to five animal species including man. Urinalyses for free and peptide-bound amino acids were made. Four adult male human subjects given orally 30 g of gelatin showed significant increases in urinary peptide-bound proline and hydroxyproline and free
hydroxylysine as compared to a casein control diet. No changes in free proline or hydroxyproline excretion were observed.

Hoffman and Kozoll (19) studied the urinary excretion of intravenous doses of 1000 ml of 5 percent osseous gelatin administered to 42 normal human male subjects. Three gelatins of weight-average molecular weights 37,000, 47,000 and 58,000 were used. Six hours after injection the amount of gelatin excreted was determined to be inversely related to the molecular weight. After 72 hours, 80 percent of all three gelatins had been excreted, although some excretion was still observable after four or five days; the authors concluded that little gelatin appeared to have been catabolized. No adverse effects were reported.

Toxicity

There are no acute toxicity studies reported. However, much research on the nutritional value of gelatin has shown that high concentrations in the diet retarded growth and produced fatalities unless the inadequacies in amino acids were balanced through other sources. For example, Jackson et al. (20) fed 25 rats weighing 78 to 114 g, a diet containing 35 percent gelatin (35 g per kg body weight) supplemented with tyrosine (0.9 percent), cystine (0.5 percent), and tryptophan (0.35 percent). Half of the animals died within 9 to 48 days, since as is now known, the diet was inadequate in threonine and methionine and even other amino acids.

MacKay and MacKay (21) studied the relationship of level of protein intake and kidney weights in male albino rats fed various proteins from 26 to 70 days of age. They found that rats on diets containing 30 to 50 percent gelatin in combination with 16 percent casein grew poorly, but showed significant increases in kidney size; histologically, the kidneys appeared normal. Although the authors inferred that enlargement represented an early state of renal damage owing to the feeding of gelatin it is likely that enlargement was due to the need to excrete large amounts of amino acid nitrogen from the feeding of a large quantity of a poor quality protein rather than to a direct nephrotic effect of gelatin.

Short-term studies

Reports in the literature over the past half-century attest to the inadequacies of dietary gelatin as a nutritional protein source. A wide variety of diets received attention: gelatin alone, gelatin plus amino acid supplements, and gelatin supplemented with various other proteins.

Diets containing casein or gelatin were studied by Ramakrishnan (22); 80 g rats fed 20 percent casein for 25-28 days grew satisfactorily, while those fed 16.5 percent gelatin (about 15 g per kg of body weight) for 20-25
days lost 20 g in weight and suffered from inanition. Liver xanthine oxidase
determination showed 70 percent less activity in the gelatin fed rats than
those fed the isonitrogenous casein diet. Methionine supplements (532 mg
percent DL-methionine) in the gelatin diet doubled the xanthine oxidase
activity, but did not affect the depressed growth rate.

Nilson and Lemon (23) fed 4-week-old rats basal diets containing
15 percent casein, 5 percent lactalbumin, 5 percent brewers yeast, and 2 per-
cent wheat germ. Five to 30 percent gelatin, bone or pig skin, was incor-
porated in the basal diet retaining approximately enough casein and lactal-
bumin to balance the amino acid deficiencies of gelatin. Mean daily growth
rates were determined for a 10-week feeding period. Growth depression was
noted on all diets which contained gelatin and was approximately proportional
to the gelatin level. Growth depression was 17 percent at 5 percent gelatin
in the diet and 75 percent at the 30 percent level. No difference was observed
between bone and pig skin gelatins. The group of rats fed the control diet
and the combined groups which had previously been fed the 5 and 10 percent
levels of gelatin were fed the 5 percent gelatin diet for over two years.
Deaths were finally due to pneumonia and malignant tumors. The authors
did not retain animals on a control diet and give no information on the inci-
dence of malignancies.

Ricceri (24) noting that diets deficient in one or more essential amino
acids result in lowered allantoin excretion regardless of which particular
amino acid is missing, studied the purine metabolism of rats given diets
deficient in essential amino acids. Male, adult albino rats were pair-fed
a diet containing 18 percent casein as a control; the casein was replaced by
gelatin during a deficiency period and when the gelatin diet was supplemented
with essential amino acids. Comparisons were drawn by analysis of the urine
for allantoin as well as uric acid, total nitrogen and creatinine. Four-stage
diets were utilized: casein alone for a period, then gelatin alone, then gelatin
plus tryptophan, cystine, and a mixture of leucine, isoleucine, methionine
and tyrosine added in that order, and finally casein alone. Each amino acid
was added in such quantity that it amounted to 5 percent of the protein content
of the diet. Total feeding period for each of 2 pairs of rats was 62 days.
Analytical results for allantoin, uric acid and creatinine for each of the four
stages followed similar patterns; first a normal value, then a marked
decrease in values followed by a slow increase to normal which was only
attained after the addition of all of the amino acids, and in the final stage, a
continuation of normal values on the casein diet.

Except for studies of Nilson and Lemon (23) reported above, no long-
term feeding studies have been found on gelatin. As indicated above, unless
supplemented with the amino acids in which it is deficient, gelatin will not
sustain life.
Maurer (25) injected human volunteers with gelatin and oxypolygelatin and showed not only antibody production but also the presence of antibodies in the preimmunization sera. Ratner and Crawford (26) using guinea pigs performed anaphylactic studies on comminuted crude bovine ossein, crude gelatin prepared from the crude ossein, commercial food grade gelatin, and intravenous grade bone gelatin, and concluded they were non-anaphylactogenic. Randolph (27) reported observing allergic signs in human patients who were sensitive to beef. Ingestion of osseous gelatin by these patients produced severe reactions in three of four tested; the fourth showed no reaction, as did four patients who were not beef-protein sensitive. The signs were nasal stuffiness, nausea, diarrhea, tinnitus and cramps. The same patients showed no reactions when tested with commercial porcine gelatin. Mendez and Hughes (28) reported on a female patient who suffered from urticaria and angioneurotic edema after ingesting boiled and stewed meats or gravies made from meat stock as well as ice cream and jellies. Extracts from gelatin and food containing gelatin all produced positive allergic reactions. Desensitization with gelatin caused the clinical allergic signs to disappear. Circulating antibodies were present in the patients' serum. Among 1000 allergic individuals tested about 1 in 150 gave positive skin reactions to gelatin and only 1 in 500 showed a clinical sensitivity, leading the authors to conclude that gelatin was a rare allergen in man.

Pietra et al. (29) injected 3 groups of Swiss albino mice with 1 percent gelatin solution: 17 newborn with 0.02 ml subcutaneously; 20 newborn with 0.02 ml intraperitoneally and 15 eight-week-old mice with 0.45 ml subcutaneously. Incidence of tumors did not differ from that in control animals. Flaks (30) injected subcutaneously in the interscapular region Strong A and C57B1 mice, 3 groups of each strain, 50 per group -- newborn, 7-day and 14-day-old -- with 15 ml of 3 percent aqueous gelatin solution. At 52 weeks incidence of tumors did not differ significantly from untreated control animals. Similarly, Roe et al. (31) found no difference at 36-43 weeks after injection in the incidence of tumors in BALB/C mice between 49 untreated controls and 28 that were injected, newborn, subcutaneously in the interscapular region, with 0.02 ml of 1 percent aqueous gelatin solution.

Teratogenicity, mutagenicity and drug interaction data were lacking in the material available to the committee for consideration.

V. OPINION

Gelatin is a hydrolyzate of naturally occurring collagen, an ingredient of commonly consumed foods of animal origin. It has been used for over 125 years as an ingredient in the manufacture of various foodstuffs.
There is no documented evidence of a deleterious nature to humans from the ingestion of gelatin, other than a rare allergic response, when the diet has provided an adequate amount of the amino acids in which gelatin is deficient. It completely lacks the essential amino acid tryptophan and is deficient in several others, and thus is of low nutritive value. Gelatin is used in various pharmaceutical formulations. The incidence of tumors in experimental animals (mice) injected subcutaneously with gelatin in various strength solutions, did not differ from that in untreated control animals.

No significant adverse findings other than rare hypersensitivity have been found in the examination of data from feeding and biochemical experiments. Thus, there is no evidence to demonstrate a hazard to the public at the level gelatin is consumed as a food or a food ingredient.

Based on these considerations, the Select Committee concludes that:

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


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