EVALUATION OF THE HEALTH ASPECTS OF GUM TRAGACANTH

AS A FOOD INGREDIENT

DECEMBER, 1972

Prepared for

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

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

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

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

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

C. Jelleff Carr, Ph. D.
Director
Life Sciences Research Office
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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 gum tragacanth 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 December 1972. Gum tragacanth is one of the food substances 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 January 1, 1972).

As indicated in the Food, Drug and Cosmetic Act [21 USC 321 (s)], GRAS substances are exempt from the requirement of premarketing clearance for food additives. It is stated in 21 CFR 121.1 that GRAS means general recognition of safety by experts qualified by scientific training and experience to evaluate the safety of substances on the basis of scientific data derived from published literature. This section of the Code also indicates that expert judgment is to be based on the evaluation of results of credible toxicological testing, or for those substances used in food prior to January 1, 1958, on a reasoned judgment founded in experience with common food use, and is to take into account reasonably anticipated patterns of consumption, cumulative effects in the diet, and safety factors appropriate for the utilization of animal experimentation data. It is recognized further (21 CFR 121.3) that it is impossible to provide assurance that any substance is absolutely safe for human consumption.

The Select Committee on GRAS Substances of LSRO is making its evaluations of these substances in full recognition of the foregoing provisions. In reaching its decisions the Select Committee, with the concurrence of FDA, is relying primarily on the absence of substantive evidence indicating the existence of a significant risk to the public health, and realizes that a decision, based on reasoned judgment, is expected even in instances where the available information is qualitatively or quantitatively limited.

In this context, the LSRO Select Committee on GRAS Substances has reviewed the available information on gum tragacanth and submits its interpretation and assessment in this report, which is intended for the use of FDA in determining the future status of gum tragacanth under the Federal Food, Drug and Cosmetic Act.
II. BACKGROUND INFORMATION

Gum tragacanth is the dried exudate from several species of Astragalus, a shrub that grows wild in mountainous regions of the Middle East, particularly in Iran. The gum is obtained by making incisions in the tap roots of the plant; to a lesser extent, the branches also are tapped. The gum exudes in the form of curled ribbons or flakes which become horny on drying. Collections are made by hand from May to October and brought to trading centers, then to wholesale markets, where the material is sorted, graded, packed, and shipped. The processor then further grades, cleans, mills, and blends the gum, and sells it in the form of ribbons, flakes, granules, or powder (1, 8).

Tragacanth is a complex mixture of polysaccharides containing galactose, fucose, xylose, arabinose, and a uronic acid, whose structure is incompletely established. The acidic components are largely present as calcium, magnesium, and potassium salts. The molecular weight is variously reported as 310,000 and 840,000. Tragacanth is considered to contain two primary constituents, tragacanthin and bassorin. The lesser component, tragacanthin, which is water-soluble, has a ring containing three molecules of a uronic acid and one molecule of arabinose, with a side chain of two molecules of arabinose. The larger component, bassorin, which swells but is insoluble in water, is believed to contain polymethoxylated acids that yield tragacanthin upon demethoxylation (1, 7, 8).

Specifications for gum tragacanth in the Food Chemicals Codex set maximum limits for arsenic (3 ppm), lead (10 ppm), heavy metals as lead (40 ppm), total ash (3.0 percent), and acid-insoluble ash (0.5 percent). The minimum viscosity of a 1 percent solution is set at 250 centipoises (5).

The history of tragacanth predates the Christian era by several centuries (8); however, 1925 was apparently the year of its first use in the United States as a food ingredient (3).

In the food industry, gum tragacanth is reported to be used principally as a stabilizer or thickening agent, in proportions ranging from 1.3 to 0.004 percent. It is currently used in the following food categories, arranged in decreasing order of content: fats and oils, gravies, condiments and relishes, meat products, baked goods, processed fruit, poultry, fish products, gelatin puddings, nonalcoholic
beverages, processed vegetables, soft candy, frozen dairy products, fruit ices, and hard candy (3). The Select Committee has no information to indicate whether the tragacanth content of any of these food categories has changed significantly in recent years, or is likely to change in future.

Some indication of the total consumption of gum tragacanth is provided by a survey conducted by a subcommittee of the National Research Council (3), which showed that in 1970 the use of gum tragacanth for food purposes in the United States was about 1.52 million pounds. Comparative figures are provided in Census Bureau reports (4), which indicate that from 1964 through 1971, imports of gum tragacanth for all purposes were 1.36, 1.32, 1.79, 3.73, 1.77, 1.79, 1.71, and 1.55 million pounds, respectively. The average for these eight years is 1.88 million pounds.

III. CONSUMER EXPOSURE DATA

The NRC survey (3) has provided information on the possible daily human intake of gum tragacanth 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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Average</td>
<td>Maximum</td>
</tr>
<tr>
<td>0-5 mos.</td>
<td>15</td>
<td>35</td>
</tr>
<tr>
<td>6-11 mos.</td>
<td>159</td>
<td>409</td>
</tr>
<tr>
<td>12-23 mos.</td>
<td>315</td>
<td>648</td>
</tr>
<tr>
<td>2-65+ yrs.</td>
<td>574</td>
<td>1155</td>
</tr>
</tbody>
</table>

*Calculations based on an average weight of 60 kg for an adult (9) 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 (6).
It is recognized that in the age group 2-65+ years, the figures for daily intake of gum tragacanth per kilogram of body weight could be deceptively low, since most individuals from age 2 years to maturity will probably weigh less than 60 kg; thus the daily intake of gum tragacanth by children could be significantly higher than the figures indicate. However, such deviations from the figures in the table must also be considered in respect to total production and use of gum tragacanth. The NRC subcommittee has pointed out that its calculations of intakes in most cases are overstated, often by considerable margins.* That human intakes are undoubtedly overstated in the case of gum tragacanth is borne out by the following calculation: The NRC subcommittee has also provided data (3) to show that the use of tragacanth for food purposes in the United States was 915,589 pounds (416,177 kg) in 1970. This figure is reported to comprise between 60 and 70 percent of the total actual poundage used in food. On the basis of 60 percent adjusted to 100 percent (693,627 kg), and a U.S. population of 200 million, the per capita per day average intake would be 10 mg instead of the 574 mg indicated in the table. The derived total of 693,627 kg of gum tragacanth used in foods per annum appears reasonable, since Census Bureau import statistics (4) show that only an average 852,000 kg of gum tragacanth are imported annually for all purposes. These figures suggest that not nearly enough gum tragacanth is imported, even if all were used in food, to reach daily intakes as high as is indicated in the foregoing table.

On the basis of these considerations, therefore, the Select Committee regards the figures in the table as levels that are highly unlikely to be achieved by any of the age groups, but more likely are generous overestimates of the gum tragacanth content of the daily diet.

*An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee report (4). The Select Committee finds this explanation reasonable and concurs in the first recommendation of Section XII of the same report that "in order to conduct a more accurate survey on the intake of substances used in food processing, food consumption data collected specifically for this purpose are needed."
IV. BIOLOGICAL STUDIES

The literature contains few references to the biological activity of gum tragacanth. In work reported, the toxicology of the substance generally has been subordinated to other interests.

Kratzer and coworkers have studied the nutritive value of gum tragacanth in poultry feeds, in comparison with other sources of carbohydrate (16). A control group of day-old chicks was fed a nutritionally-balanced stock diet, ad lib. Test groups received the stock diet modified with 2 percent gum tragacanth. After three weeks, the chicks receiving tragacanth exhibited a 34 percent depression of the growth rate. Similar effects were noted in separate tests of chicks receiving guar gum, carob bean gum, gum karaya, carrageenan, dried okra, or psyllium husk. The growth depression was not attributed to dilution of the energy content of the diet, inasmuch as the addition of 2 percent cellulose to the stock diet caused little or no depression. The cause of the inhibitory effect was not reported.

Galbraith et al. (12) investigated the mechanism whereby tragacanth powder inhibits ascites tumor growth in mice. The evidence indicated that tragacanth acts indirectly as a mitotic block by becoming attached to the cellular membrane. The observed effects occurred in the interphase or early prophase cell.

Riccardi et al. (15) showed that gum tragacanth fed to cockerels at a level of 3 percent, together with 3 percent cholesterol, inhibited the development of hypercholesterolemia.

Gum tragacanth is known to induce an allergic response by ingestion, contact, or inhalation; with respect to the incidence or severity of these reactions, it resembles many allergens commonly encountered in the diet. Cases of sensitivity to tragacanth are reported by Gelfand (13,14) and by Brown and Crepea (10). The latter workers state that very small amounts of tragacanth (0.5 mg per kg of body weight, daily for a week) can cause severe symptoms when ingested by susceptible individuals. Also, they report that among the gums, the three most common allergens, in order, are acacia (arabic), karaya, and tragacanth.
Zawahry et al. in 1963 reported (17) that tragacanth powder, given orally in the amount of 3 g per day to patients suffering from dermatitis, had markedly antiallergenic therapeutic value. They also stated that an amount equivalent to 150 times the therapeutic dose, given orally to mice for 15 days, caused no deaths; however, the data given in the report were insufficient to permit an evaluation of the experimental method, results, or conclusions.

In 1969, Frohberg et al. (11) reported lethal effects of tragacanth on mice; however, subsequent investigation indicated that metabolic products or enteric bacteria were responsible for the lethality.

Perhaps the most significant observations on toxicity of gum tragacanth are a byproduct of research on the teratogenicity of the substance, conducted by Food and Drug Research Laboratories under contract from FDA (2). Pregnant animals were fed by oral intubation with suspensions of gum tragacanth at the following levels:

- Mice, 1200 mg per kg for 10 consecutive days;
- Rats, 210 mg per kg for 10 consecutive days;
- Hamsters, 900 mg per kg for 5 consecutive days;
- Rabbits, 33 mg per kg for 13 consecutive days;

At these levels, there was no discernible effect on nidation or on maternal or fetal survival; the number of abnormalities seen in both soft and skeletal tissues of the test groups did not differ from the number occurring spontaneously in sham-treated controls. However, at higher levels of feeding, significant toxic effects were produced in some groups of animals, as follows:

1. In pregnant rats dosed at 1200 mg per kg, significant maternal toxicity ensued with loss of 6 out of 22 pregnant rats. Death was accompanied by severe diarrhea and urinary incontinence with anorexia in the terminal 48 to 72 hours. At autopsy, there were no gross pathological findings apart from marked petechial hemorrhage in the mucosae of the small intestine. Rats that survived this high dose, and bore living young to term, remained outwardly normal and the offspring were likewise normal in all respects.
(2) In pregnant rabbits dosed at 150 and 700 mg per kg, significant maternal toxicity ensued with the loss of a majority of the animals. In all other respects, the foregoing observations on pregnant rats applied to the rabbits.

No studies of the carcinogenicity or mutagenicity of gum tragacanth have come to the attention of the Select Committee.

V. OPINION

Since uncertainties exist with respect to the prevalence of allergies to gum tragacanth, additional experiments should be undertaken to evaluate the significance of its allergenic effects. A statistically-significant survey, conducted by practicing allergists, would help to determine whether significant numbers of persons are being placed in a state of receptiveness to cross-reactive allergies based upon lifelong daily exposures to gum tragacanth and the other two gums alleged to be allergenic -- gum arabic and karaya gum.

Gum tragacanth, fed at relatively high levels, is reported to be toxic to pregnant animals of some species; hence, it may be advisable, in due course, to conduct feeding studies in several animal species, including pregnant animals, at dosage levels that approximate and exceed the current estimated maximum daily human intake.

The Select Committee has weighed the foregoing and concludes that:

The available information contains no evidence demonstrating that gum tragacanth constitutes a hazard to the public when used in the manner and quantity now practiced.
VI. REFERENCES CITED


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Report submitted by:

March 14, 1973

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Select Committee on GRAS Substances