Ref. 2

PB-234 904

EVALUATION OF THE HEALTH ASPECTS OF GUM ARABIC AS A FOOD INGREDIENT

FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY

PREPARED FOR
FOOD AND DRUG ADMINISTRATION

MARCH 1973

DISTRIBUTED BY:
NTIS
National Technical Information Service
U. S. DEPARTMENT OF COMMERCE

BIBLIOGRAPHIC DATA SHEET	1. Report No. FDABF-GRAS-207	2. PB 234 904

4. Title and Subtitle: Evaluation of the Health Aspects of Gum Arabic as a Food Ingredient	5. Report Date: March 1973 6.
7. Author(s)	8. Performing Organization Rept. No. SCOGS-1
9. Performing Organization Name and Address: Life Sciences Research Office, Federation of American Societies for Experimental Biology, 9650 Rockville Pike, Bethesda, Maryland 20014	10. Project/Task/Work Unit No. 11. Contract/Grant No.: FDA 72-85
12. Sponsoring Organization Name and Address: Food and Drug Administration, 200 "C" Street, S.W., Washington, D.C. 20204	13. Type of Report & Period Covered: Final-1920 to date 14.
15. Supplementary Notes	

16. Abstracts

This report, by a group of qualified scientists designated the Select Committee on GRAS Substances (SCOGS), provides an independent evaluation of the safety of gum arabic, when used in food at present or projected levels of use.

17. Key Words and Document Analysis. 17a. Descriptors

17b. Identifiers/Open-Ended Terms

17c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages
Release unlimited	UNCLASSIFIED	22
	20. Security Class (This Page) UNCLASSIFIED	22. Price $3.00

SCOGS-1

EVALUATION OF THE HEALTH ASPECTS OF GUM ARABIC AS A FOOD INGREDIENT

MARCH, 1973

Prepared for

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

Contract No. FDA 72-85

Life Sciences Research Office
Federation of American Societies
for Experimental Biology
9650 Rockville Pike
Bethesda, Maryland 20014

ia

NOTICE

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

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

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

C. Jelleff Carr

C. Jelleff Carr, Ph. D., Director
Life Sciences Research Office
FASEB

CONTENTS

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 arabic as a food ingredient, primarily on the basis of information contained in five monographs furnished by FDA (1, 2, 3, 4, 5), summarizing the world's scientific literature from 1920 through 1970, and in certain supplemental documents available as of March, 1973. Gum arabic 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 January 1, 1972).

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

The Select Committee on GRAS Substances of LSRO is making its evaluations of these substances in full recognition of the foregoing provisions. In reaching its conclusions on safety the Select Committee, in accord with FDA's guidelines, is relying primarily on the absence of substantive evidence of or reasonable grounds to suspect a significant risk to the public health, and realizes that a decision, based on such reasoned judgment, is expected even in instances where the available information is qualitatively or quantitatively limited. The Committee is also aware that biological testing, like all of science, is dynamic. Accordingly, the Committee's decisions, based as they are on the information now available, cannot anticipate and be guided by experiments

not yet done or by the results of tests that may be reconducted, using new technologies that are constantly being evolved. These decisions will need to be reviewed as new or better information becomes available.

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

II. BACKGROUND INFORMATION

Gum arabic, also called gum acacia, consists of the dried exudate from trees of various species of the genus *Acacia*, family *Leguminosae*, which grow in arid and semi-arid regions throughout the world. The gum is collected and marketed in many countries but the principal U. S. supplier is the Republic of Sudan, where the major source is *Acacia senegal* (*Acacia verek*). Gum arabic is produced when the tree is stressed by infection, poor nutrition, heat, or lack of moisture. The gum exudes through wounds in the bark that occur naturally or are purposely made to stimulate production. The exudate dries rapidly, is collected as hardened drops or "tears," sorted, graded, and marketed (1, 6). The gum becomes harder during storage; there are market preferences for both the harder (old) and softer (new) gum (1).

Chemically, gum arabic is a complex polysaccharide containing calcium, magnesium, and potassium. It has been described as heteropolymolecular, since the polymer can vary with respect to the monomer (galactose, arabinose, rhamnose, glucuronic acid, or 4-0-methylglucuronic acid) and in the mode of linking of the monomer units (6). The molecular weight also varies widely, depending on the structure which in turn depends upon the species from which the gum is derived (7). The molecular weight of the exudate from *Acacia senegal*, the gum arabic most commonly used in the United States, is reported to be about 600,000 (8). Gum arabic is unique among hydrocolloids in that it is almost completely soluble in water, facilitating its use as a stabilizer, emulsifier, and thickening agent in foods (7). Probably the

oldest and best known of the vegetable gums, arabic, apparently was first used in food in the United States in 1880 (7,9).

The Food Chemicals Codex limits water insoluble matter in the food grade gum to not more than 1 percent and moisture to not more than 15 percent; impurity content is limited to: arsenic, 3 ppm; heavy metals (as lead), 40 ppm; lead, 10 ppm (10).

Gum arabic is currently used in amounts ranging from 45 to 0.004 percent in the following food categories, arranged approximately in decreasing order of content: soft candy, hard candy (28 percent), chewing gum (2.8 percent), snack foods (2.8-0.6 percent), imitation dairy products, frostings, fats and oils, grain products (1 percent), sugar substitutes, fruit ices, nut products, gelatin puddings (0.5-0.06 percent), baked goods, meat products, alcoholic beverages (0.15-0.06 percent), instant coffee and tea (0.08-0.01 percent), nonalcoholic beverages (0.06-0.04 percent), processed fruit, frozen dairy products, breakfast cereals (0.02-0.007 percent), condiments and relishes, milk products (0.004 percent), and soups (9).

While the total poundage of gum arabic used by the U. S. food industry in 1970 was about three times that used in 1960 (9), the Select Committee has no information to indicate the extent to which the gum arabic content of the foregoing food categories has changed during the past decade.

III. CONSUMER EXPOSURE DATA

A comprehensive survey by a National Research Council subcommittee has provided information on the possible daily human intake of gum arabic in the total diet, as shown in the following table for individuals in various age groups (9). The Select Committee has converted these figures to possible intake per kilogram of body weight.

Age group	Possible daily intake			
	Total		Per kilogram of body weight*	
	Average	Maximum	Average	Maximum
	mg	mg	mg	mg
0-5 mos.	69	576	14	115
6-11 mos.	857	2578	107	322
12-23 mos.	1404	3620	128	329
2-65+ yrs.	2470	6762	41	113

*Calculations based on an average weight of 60 kg for an adult (11) 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 (12).

It is recognized that the figures calculated for the daily intake of gum arabic per kg of body weight in the age group 2-65+ years could be low for some, since most individuals from age 2 to maturity will obviously weigh less than 60 kg; thus the daily intake of gum arabic per kg for a 20 kg child, for example, could be higher by a factor of 3 than the figures indicated in the table.

However, such deviations from the figures in the table must also be considered in respect to total use of gum arabic in foods in the United States. The NRC subcommittee has pointed out that its calculations of the intakes included in the foregoing table are overstated in most cases, often by considerable margins.* That this is true in the case of gum

---

*An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee's report (9). 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."

arabic is supported by other NRC data (9) which indicate that 17,377,423 pounds (7,898,829 kg) were used for food purposes in the United States in 1970. On the basis of this figure and a U. S. population of 200 million, per capita per day average intake of gum arabic would be 108 mg rather than the 2,470 mg indicated in the table. Moreover, Bureau of the Census (13) statistics show that gum arabic imports over the past five years have varied from about 25 to 30 million pounds annually. Even if one assumes that all of the 30 million pounds (13.6 million kg) imported in 1971 were used in food, the per capita per day average intake would not exceed 187 mg.

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 gum arabic content of the human diet.

The Joint FAO/WHO Committee on Food Additives (14) indicates the acceptable daily intake of gum arabic as unlimited.

IV. BIOLOGICAL STUDIES

Absorption and Metabolism

The available information does not establish clearly the fate of ingested gum arabic. In one study, rats were fed for one week on a basal ration supplemented with various levels of gum arabic (15). Using a method involving restricted food and caloric intakes, gum arabic fed to weanling male Sprague-Dawley rats at dietary levels of 0.5 g per day and 2 g per day was shown to have caloric values of 131 percent and 110 percent of corn starch, respectively (15). In a similar study, gum arabic fed to weanling rats at a level of 1 g per day was shown to have a caloric value 75 percent that of sucrose (16). While both of these studies suggest absorption of gum arabic or some digestion product, an earlier study did not support these observations (17). Using a test for glycogenesis rats were fed high levels (34 percent gum arabic) in a single meal. Seventy-two hours later, hepatic glycogen levels were determined. It was concluded that the difference in liver glycogen between the control and gum-fed rats was insignificant (17).

As in the rat, the guinea pig appears to have some ability to utilize gum arabic for energy. Two feeding studies (18, 19) have indicated that gum arabic exhibits growth-promoting effects. In one study (18), 89 to 95 percent digestibility was reported, while in the other (19), about 70-80 percent of normal growth rate was reported and the investigators appeared to emphasize the need for the intact gum molecule.

The rabbit also appears to be able to utilize gum arabic. A total caloric value for gum arabic slightly greater than that for starch has been reported (20). In the same study, evidence for glycogenesis was demonstrated.

In one study with humans (21), no evidence for absorption of the intact gum molecule was found. In this study, 22 infants 1 to 15 months old were fed 15 to 20 g per day of gum arabic in milk. No urinary pentose excretion was observed, while significant excretion of gum arabic occurred in the stools.

It would appear, then, that gum arabic is capable of being digested to simple sugars in herbivores, and to some extent in omnivores such as man. After absorption, the digestion products are available for oxidation. Conclusive evidence indicating that the intact gum arabic molecule is absorbed under normal conditions is lacking.

Short-term studies

Several short-term feeding studies have been made with laboratory animals. In one (19), the animals were fed a synthetic diet for 6 weeks and the effects of various supplements were noted. The animals on a gum arabic supplement showed a slightly lower growth rate than did the control animals. Similar results were obtained in a succeeding study in which the effects of various mineral supplements were noted (22). In both studies it appears that the basal ration was deficient in some way. In spite of this, gum arabic tended to improve growth rate. When the influence of feeding gum arabic on the intestinal synthesis of vitamin B_{12} was examined (23), it was shown not only to permit growth in guinea pigs but also to promote the intestinal synthesis of the vitamin. In rabbits the ingestion of diets providing 20 percent by weight of gum arabic permitted significant growth with no evidence of deleterious effects (24).

Studies in mice, rats, hamsters, and rabbits showed no clearly discernible teratological effects with oral doses of gum arabic up to 1600 mg per kg per day in mice, rats, and hamsters, and up to 37 mg per kg per day in rabbits, when each animal was treated daily for 10 days (5 days in hamsters and 13 days in rabbits), starting at the sixth day of gestation (25). However, at a dose level of 800 mg per kg per day in rabbits, a majority of the dams died.

No mutagenic effect was noted in the recombination frequency in a host-mediated assay in mice, and no mutagenic effects were noted in a dominant lethal gene test in rats (26). However, a moderate effect was observed in the cytogenetic effect assay in bone marrow after *in vivo* treatment with 5.0 g per kg and 2.5 g per kg in rats. In general, these represented chromosomal breaks rather than recombinations and occurred within six hours after treatment. Similar effects were found in *in vitro* tissue cultures of human embryonic lung cells.

Neither oral LD_{50} values nor long-term gum arabic feeding studies have been reported.

Other studies

There are several reports on the effect of parenterally administered gum arabic in man and other animals.

Treatment with intraperitoneal doses of gum arabic three times per week for up to 15 weeks in rats revealed no evidence of carcinogenicity (27). Solutions in saline or water containing 1.75 or 7.00 percent gum arabic were used. The size of dose is difficult to ascertain from the data presented, but it appears that levels were of the order of several hundred mg per kg. In a similar study with mice, no carcinogenic effect was noted, but amounts of gum arabic injected are not indicated (28). Injection of as much as 4.8 g of gum arabic per kg in dogs elicited no evidence of toxic effects but the same dose level killed dehydrated dogs, the highest no effect level being 1.9 g per kg (29).

The intravenous LD_{50} of sodium arabinate, specially prepared from calcium arabinate by alcohol precipitation from an aqueous sodium chloride solution, can be estimated as 1 g per kg in rabbits from data reported (30). The effect of single and repeated intravenous doses of gum arabic solution in dogs was investigated (31). Total doses ranged from about 1 to 2 g per kg given over a period ranging from 1 to 84 days. The most

characteristic finding was that of enlarged livers and swollen kidneys. Similar levels of gum arabic were fatal to two rabbits (31).

A similar study in which doses ranging from 16 to 48 g per kg were given intravenously over 76 days to three dogs showed gum arabic to be stored in the liver for as much as 2 years after cessation of dosing in the two dogs that survived. The dog administered gum arabic at the level of 48 g per kg died 6 months after cessation of the treatment. No functional hepatic injury was noted, but large amounts of gum arabic were found in the liver (32).

Hospitalized patients have received gum arabic solutions intravenously as a part of therapy in an attempt to develop a blood plasma substitute in the treatment of shock (33, 34, 35). These early trials conducted between 1922 and 1937 proved unsuccessful. They do provide an estimate of the intravenous acute toxicity of this relatively crude substance for man to be of the order of 150 to 600 mg per kg.

Other human studies on patients with nephrosis, as well as studies on dogs and rabbits, showed that intravenously injected gum arabic or some product associated with it accumulated in the liver and remained in the tissues for several months (36). Non-lethal effects included serious disturbances in hemoglobin, white blood cells, and serum proteins. These investigators also noted that in the nephrotic patient about 20 percent of the gum arabic injected over a period of 6 weeks was excreted in the urine. Similar accumulation effects have been noted in other animal studies (37, 38, 39). Studies have also been reported to indicate the mobilization of gum arabic from storage in various organs (40).

These observations become more important when considered in terms of the possible oral allergenicity of gum arabic. Studies in animals have shown that the antigenic property of the gum is a function of the gum itself and not of a contaminant (41). Other studies have confirmed that sensitivity to gum arabic is in fact a true antibody-antigen phenomenon and not an artifact of some other metabolic event (42).

Human sensitivity to gum arabic has been suggested in a number of reports of work-associated allergic reactions to the gum (43, 44). However, the most carefully documented series of studies on human subjects and their response to oral administration of vegetable gums in general and gum arabic in particular is that of Gelfand (45). In 10 sensitive patients, vegetable gums in their food were confirmed as the allergens responsible for their sensitivity. Moreover, Gelfand was also able to show cross-sensitivity with several other gums such as tragacanth and karaya.

In general, the foregoing studies suggest a systemic effect of gum arabic when administered intravenously. Moreover, there appears to be in certain susceptible individuals significant allergic response to ingestion of this gum.

V. OPINION

In common with many other food ingredients of natural origin, commercial gum arabic is a relatively crude and undefined material. In view of the demonstrated capacity of this material as a sensitizing agent, and despite strong indications that sensitization is due to the gum polysaccharide itself, it becomes important to know, nevertheless, to what extent extraneous contaminants such as protein may be contained in the commercial product. The Select Committee suggests consideration of revising the specifications for gum arabic to establish limits for the content of materials such as protein that may possibly be associated with some of the observed biological effects of the commercial gum.

In view of the prevalence of allergies to gum arabic, and its increasing use in a wide variety of food products, additional experiments should be undertaken to evaluate the significance of its allergenicity in the population as a whole. An epidemiological survey might determine whether significant numbers of persons are being placed in a state of receptiveness to cross-reactive allergies based upon daily lifelong exposures to gum arabic and two other gums alleged to be allergenic - gum tragacanth and karaya gum.

Gum arabic, fed at relatively high levels, is reported to be toxic to pregnant animals of one 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 maximum daily human intake.

The Select Committee has weighed the foregoing and concludes that:

> There is no evidence in the available information on gum arabic that demonstrates a hazard to the public when it is used at levels that are now current and in the manner now practiced. However, it is not possible to determine without additional data, whether a significant increase in consumption would constitute a dietary hazard.

VI. REFERENCES CITED

1. TRACOR/JITCO. 1972. Monograph on gum acacia. Submitted under DHEW contract no. FDA 72-100. Rockville, Md. [116 pp].

2. The Franklin Institute Research Laboratories. 1972. Monograph on gum arabic (acacia). Submitted under DHEW contract no. FDA 72-101. Philadelphia, Pa. 86 pp.

3. Battelle Columbus Laboratories. 1972. Monograph on gum arabic. Submitted under DHEW contract no. FDA 72-102. Columbus, Ohio. 67 pp.

4. Food and Drug Research Laboratories, Inc. 1972. Monograph on gum arabic. Submitted under DHEW contract no. 72-103. Maspeth, N.Y. 39 pp.

5. Informatics, Inc. 1972. Monograph on gum arabic. Submitted under DHEW contract no. FDA 72-104. Rockville, Md. 48 pp.

6. Klose, R. E., and M. Glicksman. 1972. Gums. Pages 295-359 *in* T. E. Furia, ed. Handbook of food additives, 2nd ed. The Chemical Rubber Co., Cleveland, Ohio.

7. Glicksman, M. 1969. Gum arabic. Pages 97-111 *in* Gum technology in the food industry. Academic Press, New York, N. Y.

8. Anderson, D. M. W., and I. C. M. Dea. 1971. Recent advances in the chemistry of *Acacia* gums. J. Soc. Cosmet. Chem. 22: 61-76.

9. Subcommittee on Review of GRAS List (Phase II). 1972. A comprehensive survey of industry on the use of food chemicals generally recognized as safe (GRAS). Prepared under DHEW contract no. FDA 70-22 by Committee on Food Protection, Division of Biology and Agriculture, National Research Council. National Academy of Sciences, Washington, D.C.

10. National Research Council. 1972. Acacia (gum arabic). Pages 9-10 *in* Food Chemicals Codex, 2nd ed. National Academy of Sciences, Washington, D.C.

11. Nelson, A. A. 1954. Approximate relation of parts per million in diet to mg/kg/day (table). Assoc. Food Drug Officials Quart. Bull. 18:66.

12. Altman, P. L., and D. S. Dittmer, editors. 1972. Pages 201-202 *in* Biology data book, 2nd ed., vol. 1. Federation of American Societies for Experimental Biology. Bethesda, Md.

13. U. S. Bureau of the Census, Foreign Trade Division. 1965-1972. [Gum arabic; TSUSA no. 1883600]. U. S. foreign trade imports TSUSA commodity by country. Annual. FT 246. Government Printing Office, Washington, D. C.

14. Joint FAO/WHO Expert Committee on Food Additives. 1970. Specifications for the identity and purity of food additives and their toxicological evaluation; some food colours, emulsifiers, stabilizers, anticaking agents, and certain other substances. 13th rept. Food and Agriculture Organization of the United Nations, Rome, Italy. [36 pp.].

15. Wisconsin Alumni Research Foundation. 1965. [Hallmark pure gum arabic No. 1 U.S.P. - evaluation of caloric content]. Assay report no. 4121036. Madison, Wis. 3 pp.

16. Shue, G. M., C. D. Douglas, and L. Friedman. 1962. Nutritional studies of complex carbohydrates. Fed. Proc. Fed. Amer. Soc. Exp. Biol. 21(2):91. Abstract.

17. Monke, J. V. 1941. Non-availability of gum acacia as a glycogenic foodstuff in the rat. Proc. Soc. Exp. Biol. Med. 46:178-179.

18. O'Dell, B. L., E. R. Morris, E. E. Pickett, and A. G. Hogan. 1957. Diet composition and mineral balance in guinea pigs. J. Nutr. 63:65-77.

19. Booth, A. N., C. A. Elvehjem, and E. B. Hart. 1949. The importance of bulk in the nutrition of the guinea pig. J. Nutr. 37:263-274.

20. Iwata, H. 1933. Nutritine studies on plant gums on the formation of fat and glycogen (resume). Bul. Sci. Fakult. Terkultura Kjusu Imp. Univ. 5:367-368.

21. Bentivoglio, G. C. 1931. Does gum arabic undergo intestinal absorption in the feeding infant? Boll. Accad. Med. Roma. 57:113-122. (In Italian; translation supplied with reference no. 1).

22. Roine, P., A. N. Booth, C. A. Elvehjem, and E. B. Hart. 1949. Importance of potassium and magnesium in nutrition of the guinea pig. Proc. Soc. Exp. Biol. Med. 71:90-91.

23. Wichmann, K., M. Salminen and P. Roine. 1954. On the intestinal synthesis of folic acid and biotin in the guinea pig. Suom. Kemistilehti B. 27(2):5-9.

24. Hove, E. L., and J. E. Herndon. 1957. Growth of rabbits on purified diets. J. Nutr. 63:193-199.

25. Food and Drug Research Laboratories, Inc. 1972. Teratologic evaluation of FDA 71-15 (gum arabic) in mice, rats, hamsters and rabbits. Maspeth, N. Y. [56 pp.]

26. Stanford Research Institute. 1972. Study of mutagenic effects of gum arabic (FDA 71-15). Compound report no. 3 prepared under DHEW contract no. FDA 71-267. Menlo Park, Calif. 31 pp.

27. Miller, E. C., J. A. Miller, and H. A. Hartmann. 196.. N-hydroxy-2-acetylaminofluorene: a metabolite of 2-acetylaminofluorene with increased carcinogenic activity in the rat. Cancer Res. 21:815-824.

28. Vilchez, C. A. and J. M. Echave Llanos. 1963. Action of vagotomy on the neoplastic lesions of glandular stomach produced in mice by 20-methyl-cholantrene. Naturwissenschaften. 50:305-306.

29. Walker, M. A., and N. M. Keith. 1930. The effect of a solution of acacia in restoring diminished body fluid. Amer. J. Physiol. 95:561-572.

30. Maas, J. A. 1938. The usefulness of gum arabic as an infusion liquid. Quart. J. Exp. Physiol. 28:315-322.

31. Hueper, W. C. 1942. Experimental studies in cardiovascular pathology. V. Effects of intravenous injections of solutions of gum arabic, egg albumin and gelatin upon the blood and organs of dogs and rabbits. Amer. J. Pathol. 18:895-924.

32. Smalley, R. E., M. W. Binger, J. L. Bollman, and M. H. Power. 1945. Effect of intravenously administered solution of acacia on animals. Arch. Int. Med. 76:39-46.

33. Lee, R. van A. 1922. Sudden death in two patients following intravenous injections of acacia. J. Amer. Med. Assoc. 79: 726-728.

34. Olivecrona, H. 1921. Fatality following injection of gum acacia. Acta Chir. Scand. 54:1-6.

35. Studdiford, W. E. 1937. Severe and fatal reactions following the intravenous use of gum acacia glucose infusion. Surg. Gynecol. Obstet. 64:772-784.

36. Andersch, M., and R. B. Gibson. 1934. Studies on the effects of intravenous injections of colloids. I. Deposition of acacia in the liver and other organs and its excretion in urine and bile. J. Pharmacol. Exp. Ther. 52:390-407.

37. Kendrick, A. B., R. W. Keeton, and E. F. Foley. 1938. Immediate and delayed disposal of acacia injected intravenously in the dog. Proc. Soc. Exp. Biol. Med. 39:465-467.

38. Heckel, G. P., C. C. Erickson, C. L. Yuile, and R. E. Knutti. 1938. Blood plasma proteins as influenced by intravenous injection of gum acacia. J. Exp. Med. 67:345-360.

39. Macovschi, E. 1958. Action of urease and β-amylase on urea and on starch in the presence of certain glucoprotein coacervates. Stud. Cercet. Biochim. 1:297-311.

40. Knutti, R. E., R. A. Warrick, and J. B. Goetsch. 1950. The maintenance of blood colloid: passage of stored gum acacia from the cells to the circulation after plasmapheresis. J. Exp. Med. 92:77-83.

41. Silvette, H., O. Swineford, Jr., and L. Tull. 1955. Observations on acacia as an immunizing, sensitizing, anaphylactogenic, and desensitizing antigen. J. Allergy 26:509-518.

42. Rice, C. E. 1955. An investigation of some of the factors determining the decrease in complement activity in anaphylactic shock. J. Immunol. 75:85-95.

43. Feinberg, S. M., and B. B. Schoenkerman. 1940. Karaya and related gums as causes of atopy. Wis. Med. J. 39:734-736.

44. Bohner, C. B., J. M. Sheldon, and J. W. Trenis. 1941. Sensitivity to gum acacia, with a report of ten cases of asthma in printers. J. Allergy 12:290-294.

45. Gelfand, H. H. 1949. The vegetable gums by ingestion in the etiology of allergic disorders. J. Allergy 20:311-321.

VII. SCIENTISTS CONTRIBUTING TO THIS REPORT

1. Members of the Select Committee on GRAS Substances:

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

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

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

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

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

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

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

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

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

2. LSRO staff:

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

3. Ad hoc consultant:

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

Report submitted by:

August 20, 1973
Date

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