NATIONAL TOXICOLOGY PROGRAM
Technical Report Series
No. 224

CARCINOGENESIS BIOASSAY OF TARA GUM

(CAS NO. 39300-88-4)

IN F344/N RATS AND B6C3F$_1$ MICE

(FEED STUDY)

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

NATIONAL TOXICOLOGY PROGRAM

The National Toxicology Program (NTP), established in 1978, develops and evaluates scientific information about potentially toxic and hazardous chemicals. This knowledge can be used for protecting the health of the American people and for the primary prevention of chemically induced disease. By bringing together the relevant programs, staff, and resources from the U.S. Public Health Service, DHHS, the National Toxicology Program has centralized and strengthened activities relating to toxicology research, testing and test development/validation efforts, and the dissemination of toxicological information to the public and scientific communities and to the research and regulatory agencies.

The NTP is comprised of four charter DHHS agencies: the National Cancer Institute, National Institutes of Health; the National Institute of Environmental Health Sciences, National Institutes of Health; the National Center for Toxicological Research, Food and Drug Administration; and the National Institute for Occupational Safety and Health, Centers for Disease Control. In June 1981, the Carcinogenesis Bioassay Testing Program, NCI, was transferred to the NIEHS.

NTP Technical Report

on the

CARCINOGENESIS BIOASSAY

of

TARA GUM

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in F344 RATS AND B6C3F$_1$ MICE

(FEED STUDY)

NATIONAL TOXICOLOGY PROGRAM
Research Triangle Park
Box 12233
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NOTE TO THE READER

This is one in a series of experiments designed to determine whether selected chemicals produce cancer in animals. Chemicals selected for testing in the NTP carcinogenesis bioassay program are chosen primarily on the bases of human exposure, level of production, and chemical structure. Selection per se is not an indicator of a chemical's carcinogenic potential. Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the conditions of the test and indicate that exposure to the chemical is a potential hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals requires a wider analysis which extends beyond the purview of this study.

This study was initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

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Comments and questions about the National Toxicology Program Technical Reports on Carcinogenesis Bioassays should be directed to the National Toxicology Program, located at Room A-306, Landow Building, Bethesda, MD 20205 (301-496-1152) or at Research Triangle Park, NC 27709 (919-541-3991).

Although every effort is made to prepare the Technical Reports as accurately as possible, mistakes may occur. Readers are requested to communicate any mistakes to the Deputy Director, NTP (P.O. Box 12233, Research Triangle Park, NC 27709), so that corrective action may be taken. Further, anyone who is aware of related ongoing or published studies not mentioned in this report is encouraged to make this information known to the NTP.

TABLE OF CONTENTS

TABLES

FIGURES

APPENDIXES

ABSTRACT

A carcinogenesis bioassay of tara gum, a potential stabilizer for cosmetics and foods, was conducted by feeding diets containing 25,000 or 50,000 ppm of the test substance to 50 F344 rats and 50 B6C3F1 mice of either sex for 103 weeks. Groups of 50 untreated rats and mice of either sex served as controls.

In the chronic bioassay, mean body weights of dosed and control rats of either sex were comparable over the course of the study. Feed consumption by low- and high-dose male rats was 92% and 95% that of the controls, and feed consumption by low- and high-dose female rats was 87% and 79% that of the controls. Mean body weights of high-dose mice of either sex were lower than those of controls; feed consumption by dosed mice was comparable with that of controls. Although the rats and mice might have been able to tolerate higher doses, 50,000 ppm (5%) is the recommended maximum concentration of a test substance mixed in feed, according to the guidelines of the Bioassay Program.

No tumors were observed in increased incidences that were considered to be related to administration of tara gum to either species. Interstitial-cell tumors of the testis in male rats were observed in a statistically significant ($P \leq 0.003$ for trend and group comparisons) positive relationship (40/48 controls; 46/46 low dose; 48/48 high dose); because these tumors are present in almost all aged F344 male rats and because of the marginal statistical significance when time-adjusted analyses are applied, these increases are not regarded as being related to tara gum administration.

A significant ($P < 0.05$) negative trend was observed in the proportion of male rats with pancreatic islet cell adenoma (5/45 controls, 1/44 low dose, 0/45 high dose), of female mice with alveolar/bronchiolar adenomas (7/50, 2/49, 2/50), and of female mice with hepatocellular adenomas (9/49, 4/49, 1/50).

Under the conditions of this bioassay, tara gum was not carcinogenic for F344 rats or B6C3F1 mice of either sex.

CONTRIBUTORS

The bioassay of tara gum was conducted at EG&G Mason Research Institute, Worcester, Massachusetts, under a subcontract to Tracor Jitco, Inc., the prime contractor for the NCI/NTP Bioassay Program. The prechronic study was started in November, 1976 and finished in April, 1977; the chronic study was begun in October, 1977 and completed in October, 1979.

The bioassay was conducted under the direction of Drs. H. Lilja (1) and E. Massaro (1,2), principal investigators. Doses of the test chemical were selected by Drs. J. Robens (3,4), C. Cueto (5), and R. Fogleman (3). The program manager was Ms. R. Monson (1). Ms. A. Good (1) supervised the technicians in charge of animal care, and Ms. E. Zepp (1) supervised the preparation of the feed mixtures and collected samples of the diets for analysis. Ms. D. Bouthot (1) kept all daily records of the test. Dr. A.S.K. Murthy (1), pathologist, directed the necropsies and performed the histopathologic evaluations. The pathology report and selected slides were evaluated by the NCI Pathology Working Group as described by Ward et al. (1978). The diagnoses represent a consensus of contracting pathologists and the NCI Pathology Working Group, with final approval by the NCI Pathology Working Group.

Animal pathology tables and survival tables were compiled at EG&G Mason Research Institute, Rockville, Maryland (6). The statistical analyses were performed by Dr. J. R. Joiner (3) and Mr. J. Warner (3), using methods selected for the bioassay program by Dr. J. J. Gart (7).

This report was prepared at Tracor Jitco (3) and reviewed by NTP. Those responsible for the report at Tracor Jitco were Dr. C. Cueto, (5), Director of the Bioassay Program; Dr. S. S. Olin, Associate Director; Dr. M. A. Stedham, pathologist; Dr. J. Tomaszewski, chemist; Dr. W. D. Theriault, reports manager; Dr. A. C. Jacobs, bioscience writer; and Ms. C. E. Dean, technical assistant.

The following scientists at NTP (8) were responsible for evaluating the bioassay experiment, interpreting the results, and reporting the findings: Dr. J. Fielding Douglas, Dr. Charles K. Grieshaber (chemical manager), Dr. Joseph Haseman, Dr. James Huff, Dr. C. W. Jameson, Dr. Ernest E. McConnell, Dr. John A. Moore, Dr. Sherman F. Stinson, Dr. R. Tennant, and Dr. Jerrold M. Ward.

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PEER-REVIEW PANEL AND COMMENTS

On February 18, 1981, this carcinogenesis bioassay report on tara gum underwent peer review and was approved by the National Toxicology Program Board of Scientific Counselors' Technical Report Review Subcommittee and associated Panel of Experts at an open meeting held in Building 31C, National Institutes of Health, Bethesda, Maryland.

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*Unable to attend February 18, 1981, meeting

Dr. Richard Waritz, Manager of Toxicology, Hercules Incorporated, made a public statement in which he expressed concern about the wording of the conclusion in the report, which said, "no evidence was found that tara gum was clearly carcinogenic for F344 rats or B6C3F1 mice of either sex." He said the use of "clearly" was apparently based on an increased incidence of interstitial-cell tumors in test rats over controls. However, when life table analysis was done to correct for early mortality of controls, there were shown to be no significant differences in the incidence of this tumor between test rats and controls. He requested that the summary and conclusion be reworded to properly reflect the non-carcinogenicity of tara gum in this bioassay.

Dr. Shore, as a prinicipal reviewer for the report on the bioassay of tara gum, agreed with the conclusion of the report except that the word "clearly" should be deleted as requested by Dr. Waritz in view of the lack of significance shown by life table analysis for the incidence of interstitial-cell tumors in rats. As to other effects, he noted an apparent excess of mineralization of the testes in male rats, and, in the subchronic study, a decreased number of mature spermatozoa in high-dose rats.

As a second principal reviewer, Dr. Hitchcock commented on the uncertainty as to the actual concentration of the test compound in the diet since quantitative methodology was lacking to enable stability testing. Regardless, she considered the study to be valid under the test conditions. Dr. Mirer requested that the life table analysis on the interstitial-cell tumors be included in the text. Dr. Haseman, National Toxicology Program, stated that in the final report, discussion of the interstitial-cell tumor analyses will give greater emphasis to procedures that take into account the early mortality in control animals. (NTP considers that time-adjusted tests are preferable to life table analyses for interstitial-cell tumors, since these lesions are generally regarded as "incidental tumors" which are not considered to be life-threatening.)

Dr. Shore moved that the report on the bioassay of tara gum be accepted with minor revision of the conclusion and summary. Dr. Hitchcock seconded the motion and the report was approved unanimously by the peer review panel.

I. INTRODUCTION

Tara gum (CAS No. 39300-88-4) is the milled endosperm of the leguminous plant Caesalpinia spinosa that is native to Peru (Anderson, 1949).

Structurally, tara gum is a galactomannan polymer consisting of a main chain of β-D-mannopyranose units with side chains of α-D-galactopyranose attached by (1-6) linkages approximately every third unit (WHO, 1975). The ratio of mannose to galactose in tara gum is intermediate between that of locust bean gum and guar gum (Anderson, 1949).

Because of its special properties as a long-flowing, cold-water-soluble gum, tara gum was considered in the early to mid 1970's as an inexpensive substitute for locust bean gum and guar gum, which are used as thickeners for water-soluble dyes, binders, and stabilizers in ice cream or cosmetic lotions (Habersberger, 1973; Dea and Finney, 1978). Tara gum has not been approved for use in foods in the United States (U.S. Bureau of Foods, 1979), but it was used in some cosmetic lotions from 1973 to 1978. By 1979, tara gum was no longer economically competitive with locust bean gum or guar gum. Consequently, tara gum is no longer being imported into the United States (Dycol Chemical Co., 1979).

In a 90-day feeding study in groups of 10 rats of either sex, the relative weights of the thyroid and of the cecum were increased in animals fed diets containing 20,000 or 50,000 ppm tara gum. An increase in the relative weight of the kidneys of male rats fed 50,000 ppm was also observed (Til et al., 1975). No other references on the toxicity of tara gum are known, and no data on its mutagenicity have been found.

Tara gum was tested by the Bioassay Program because the use of tara gum in food was being considered and because tara gum had not been tested for potential carcinogenicity in lifetime bioassays (WHO, 1975).

II. MATERIALS AND METHODS

A. Chemical

Tara gum was obtained as one batch (Lot No. 897) from Dycol Chemicals, Inc. (Bridgewater, NJ).

Analysis of the chemical was performed at Midwest Research Institute (Kansas City, MO). The entire batch was first homogenized in a Day® blender for 1 hour, and hydrolyzed samples were titrated by periodate oxidation using a modification of the USP assay for mannitol. The results indicated a purity of 86.2% as compared with dextrose. The water content, determined by Karl Fischer titration, was 12.4%. Thin-layer chromatography of the hydrolysis products in one system indicated that both mannose and galactose were produced as expected, but a third major component was never identified. Analyses in other thin-layer chromatography systems showed the presence of only mannose and galactose (Appendix E).

The infrared spectrum of the chemical was analyzed on a regular basis throughout the bioassay and showed no change.

B. Dietary Preparation

Test diets were prepared by mixing tara gum with an aliquot of powdered Wayne Lab Blox® animal feed (Table 1) with a mortar and pestle and then placing the mixture and the rest of the feed in a Patterson-Kelly® twin-shell V-blender and mixing for 10 minutes. Test diets were sealed in labelled plastic bags and stored at 4°C for no longer than 14 days.

Due to the similarity of tara gum and some components of the feed, the available quantitative analytical methods could not be used for chronic dosed-feed analyses of tara gum levels. Therefore, the stability of the compound in feed could not be routinely determined, and formulated diets were not analyzed for concentrations of tara gum during the study.

Table 1. Source and Descriptions of Materials Used for Animal Maintenance

Item	Description	Source
Animal Feed	Wayne Lab Blox® (meal)	Allied Mills (Chicago, IL)
Feed Hoppers	Stainless steel, gang style	Scientific Cages, Inc. (Bryan, TX)
Cages	Polycarbonate	Lab Products, Inc. (Rochelle Park, NJ)
Filter Sheets	Disposable, nonwoven fiber	Lab Products, Inc. (Rochelle Park, NJ)
Bedding	Hardwood chips: Aspen® bed	American Excelsior (Baltimore, MD)
	Beta® Chips	Agway Corp. (Syracuse, NY)

Historically, levels of a test substance in feed mixtures from this laboratory have been within 10% of the prescribed concentrations.

C. Animals

For the subchronic studies, 4-5 week-old B6C3F1 mice and F344 rats were obtained from the Frederick Cancer Research Center. Animals were held for 7 days before the study began. Animals were distributed to the various test groups by sex and species so that the average body weight for each cage was approximately equal.

For the chronic study, 4-week-old F344 rats and 5-week-old B6C3F1 mice were obtained from the Harlan Industries, Inc., (Indianapolis, IN) and observed for the presence of parasites and other diseases for 14 days. The animals were assigned to individual cages according to a table of random numbers and the cages were randomly assigned to test groups.

D. Animal Maintenance

Rats and mice were housed five per cage in suspended polycarbonate cages equipped with disposable nonwoven fiber filter sheets (Table 1). Hardwood chip bedding and cages were changed twice weekly, and cage racks were changed every 2 weeks. Water was supplied by an Edstrom automatic watering system, and Wayne Lab Blox® meal in stainless-steel, gang-style hoppers was available *ad libitum*.

The temperature in the animal rooms was 19°-30°C (average 23.6°C); relative humidity was not controlled. Incoming air was filtered through Tri-Dek 15/40 denier Dacron filters, with 10 to 12 changes of room air per hour. Fluorescent lighting was provided 12 hours per day.

E. Single-Dose-Toxicity and 14-Day Repeated-Dose Study

Single-dose toxicity and 14-day repeated-dose feed studies were conducted with F344 rats and B6C3F1 mice to determine the concentrations of tara gum to be used in the subchronic studies.

In the single-dose toxicity test, groups of five males and five females of each species were administered a single-dose of the test substance (0.63 g/kg body weight) in distilled water by gavage. On day 15, all animals were killed and necropsied. No compound-related effects were observed.

In the repeated-dose study, groups of five males and five females of each species were fed diets containing 0, 6,300, 12,500, 25,000, 50,000, or 100,000 ppm tara gum in feed for 2 weeks (Tables 2 and 3). On day 15, the animals were fed control diets. All animals were observed daily throughout the study and were killed and necropsied on day 16.

No deaths occurred among the rats. Mean body weight gain compared with the controls was depressed 12% or more among males receiving 50,000 or 100,000 ppm and 8% among females receiving 100,000 ppm. No other compound-related effects were noted during clinical observations or gross necropsy.

No deaths occurred among the mice. Mean body weight gain was depressed by more than 20% among dosed male mice. Male mice fed diets containing 100,000 ppm tara gum gained no weight. Mean body weight gain was depressed by 50% in females receiving 50,000 ppm. No other compound-related effects were noted during clinic observations or gross necropsy.

F. Subchronic Studies

In subchronic studies conducted to determine the concentrations of tara gum to be used in the chronic studies, groups of 10 rats and 10 mice of each sex were fed diets containing 0, 3,100, 6,300, 12,500, 25,000, or 50,000 ppm for 13 weeks (Tables 4 and 5). Mortality checks were made twice daily, and

Table 2. Dosage, Survival, and Mean Body Weights of Rats Fed Diets Containing Tara Gum for 14 Days

Dose (ppm)	Survival (a)	Mean Body Weights (grams) Initial	Final	Change	Weight Change Relative to Controls (b) (Percent)
MALE					
0	5/5	87.0	157.0	+70.0	
6,300	5/5	86.6	159.4	+72.8	+4.0
12,500	5/5	86.8	158.8	+72.0	+2.9
25,000	5/5	86.8	152.2	+65.4	-6.6
50,000	5/5	86.4	147.8	+61.4	-12.3
100,000	5/5	87.0	144.0	+57.0	-18.6
FEMALE					
0	5/5	71.8	111.2	+39.4	
6,300	5/5	71.6	110.2	+38.6	-2.0
12,500	5/5	71.4	114.4	+43.0	+9.1
25,000	5/5	72.0	112.2	+40.2	+2.0
50,000	5/5	72.0	112.7	+40.7	+3.3
100,000	5/5	71.6	107.8	+36.2	-8.1

(a) Number surviving/number per group

(b) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

Table 3. Dosage, Survival, and Mean Body Weights of Mice Fed Diets Containing Tara Gum for 14 Days

Dose (ppm)	Survival (a)	Mean Body Weights (grams)			Weight Change Relative to Controls (b) (Percent)
		Initial	Final	Change	
MALE					
0	5/5	20.6	23.4	+2.8	
6,300	5/5	20.6	22.4	+1.8	-36
12,500	5/5	20.4	22.6	+2.2	-21
25,000	5/5	20.6	21.4	+0.8	-71
50,000	5/5	20.6	22.0	+1.4	-50
100,000	5/5	20.8	20.8	0	-100
FEMALE					
0	5/5	18.0	18.4	+0.4	
6,300	5/5	17.8	19.0	+1.2	+200
12,500	5/5	17.8	18.6	+0.8	+100
25,000	5/5	17.8	18.8	+1.0	+150
50,000	5/5	18.0	18.2	+0.2	-50
100,000	5/5	17.6	18.2	+0.6	+50

(a) Number surviving/number per group

(b) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

Table 4. Dosage, Survival, and Mean Body Weights of Rats Fed Diets Containing Tara Gum for 13 Weeks

Dose (ppm)	Survival (a)	Mean Body Weights (grams) Initial	Final	Change	Weight Change Relative to Controls (b) (Percent)
MALE					
0	10/10	96.2	316.7	+220.5	
3,100	10/10	95.9	322.1	+226.2	+2.6
6,300	10/10	96.1	310.9	+214.8	-2.6
12,500	10/10	97.0	309.8	+212.8	-3.5
25,000	10/10	96.5	316.5	+220.0	-0.2
50,000	10/10	96.6	308.6	+212.0	-3.9
FEMALE					
0	10/10	85.9	201.4	+115.5	
3,100	10/10	85.7	211.8	+126.1	+9.2
6,300	10/10	86.1	205.5	+119.4	+3.4
12,500	10/10	85.7	207.2	+121.5	+5.2
25,000	10/10	85.3	206.0	+120.7	+4.5
50,000	10/10	86.0	203.4	+117.4	+1.7

(a) Number surviving/number per group

(b) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

Table 5. Dosage, Survival, and Mean Body Weights of Mice Fed Diets Containing Tara Gum for 13 Weeks

Dose (ppm)	Survival (a)	Mean Body Weights (grams) Initial	Final	Change	Weight Change Relative to Controls (b) (Percent)
MALE					
0	10/10	19.7	34.1	+14.4	
3,100	10/10	18.7	35.4	+16.7	+16.0
6,300	10/10	19.5	33.9	+14.4	0
12,500	10/10	19.4	34.1	+14.7	+2.1
25,000	10/10	19.5	36.0	+16.5	+14.6
50,000	10/10	19.8	33.0	+13.2	-8.3
FEMALE					
0	10/10	15.5	27.9	+12.4	
3,100	10/10	15.4	25.5	+10.1	-18.5
6,300	10/10	15.2	26.9	+11.7	-5.7
12,500	10/10	15.4	26.1	+10.7	-13.7
25,000	10/10	16.2	25.7	+9.5	-23.4
50,000	9/9	15.9	25.8	+9.9	-20.2

(a) Number surviving/number per group

(b) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)}}{\text{Weight Change (Control Group)}} \times 100$$

animals were weighed weekly. At the end of the 91-day study, all animals were killed. All animals were subjected to a complete gross necropsy. Histopathologic examination was carried out on tissues (Section H) from all animals in the control and highest dose groups.

Rats: No deaths occurred among the rats. During histopathologic examination, fewer mature spermatozoa were found in the testes of 4/10 male rats receiving 50,000 ppm tara gum than in the controls. No other compound-related effects were observed. Doses of tara gum selected for rats for the chronic study were 25,000 and 50,000 ppm. The maximal dose recommended for chronic feeding studies is 50,000 ppm (NCI, 1976).

Mice: None of the mice died and no compound-related effects were detected. Doses of tara gum selected for mice for the chronic study were 25,000 and 50,000 ppm.

G. Chronic Studies

The experimental design, including the test groups, doses, and durations of the chronic studies, is presented in Table 6.

H. Clinical Examinations and Pathology

Animals were observed twice daily for morbidity and mortality and were weighed monthly. Animals that were moribund and those that survived to the end of the study were killed with carbon dioxide and necropsied.

The mean body weight of each dosed or control group was calculated as

$$\frac{\text{total weight of all animals in the group}}{\text{number of animals in the group.}}$$

Feed consumption was measured per cage. The average feed consumption per animal was calculated as

$$\frac{\text{total feed consumption measured for all cages in the group}}{\text{number of surviving animals in the group.}}$$

Table 6. Experimental Design of Chronic Feeding Studies with Tara Gum in Rats and Mice

Test Group	Initial No. of Animals	Tara Gum (ppm)	Weeks on Study: Dosed(a)	Weeks on Study: Not Dosed
Male Rats				
Control(b)	50	0	0	107
Low-Dose	50	25,000	103	3
High-Dose	50	50,000	103	2
Female Rats				
Control(b)	50	0	0	106
Low-Dose	50	25,000	103	3
High-Dose	50	50,000	103	3
Male Mice				
Control(b)	50	0	0	105
Low-Dose	50	25,000	103	2
High-Dose	50	50,000	103	2
Female Mice				
Control(b)	50	0	0	105
Low-Dose	50	25,000	103	2
High-Dose	50	50,000	103	2

(a) The start dates were October 13, 1977, for rats and November 11, 1977, for mice. The kill dates were October 26, 1979, for rats and November 18, 1979, for mice.

(b) Control and dosed groups were of the same strain, sex, and age range and were from the same source and shipment. All animals of the same species shared the same room, and all aspects of animal care and maintenance were similar. Animals were randomized to dosed and control groups as described in section II.c.

Gross and microscopic examinations were performed on major tissues and on all gross lesions from killed animals and from animals found dead unless precluded in whole or in part by autolysis or cannibalization. Thus, the number of animals from which particular organs or tissues were examined microscopically varies and does not necessarily represent the number of animals that were placed on study in each group. Tissues were preserved in 10% neutral buffered formalin, embedded in paraffin, sectioned, and stained with hematoxylin and eosin. The following tissues were examined microscopically: skin, lungs and bronchi, trachea, bone and bone marrow, spleen, lymph nodes, heart, salivary gland, liver, pancreas, stomach, small intestine, large intestine, kidneys, urinary bladder, pituitary, adrenal, thyroid, parathyroid, mammary gland, prostate and seminal vesicles or uterus, testis or ovary, brain, thymus, larynx, and esophagus.

I. Data Recording and Statistical Analyses

Data on this experiment were recorded in the Carcinogenesis Bioassay Data System (Linhart et al., 1974). The data elements include descriptive information on the chemicals, animals, experimental design, clinical observations, survival, body weight, and individual pathologic results, as recommended by the International Union Against Cancer (Berenblum, 1969).

Probabilities of survival were estimated by the product-limit procedure of Kaplan and Meier (1958) and are presented in this report in the form of graphs. Animals were statistically censored as of the time they died of other than natural causes or were found to be missing; animals dying from natural causes were not statistically censored. Statistical analyses for a possible dose-related effect on survival used the method of Cox (1972) for testing two groups for equality and Tarone's (1975) extension of Cox's methods for testing for a dose-related trend. One-tailed P values have been reported for all tests except the departure from linearity test, which is reported only when its two-tailed P value is less than 0.05.

The incidence of neoplastic or nonneoplastic lesions has been given as the ratio of the number of animals bearing such lesions at a specific

anatomic site (numerator) to the number of animals in which that site is examined (denominator). In most instances, the denominators included only those animals for which that site was examined histologically. However, when macroscopic examination was required to detect lesions prior to histologic sampling (e.g., skin or mammary tumors) or when lesions could have appeared at multiple sites (e.g., lymphomas), the denominators consist of the numbers of animals necropsied.

The purpose of the statistical analysis of tumor incidence is to determine whether animals receiving the test chemical developed a significantly higher proportion of tumors than did the control animals. As part of these analyses, the one-tailed Fisher exact test (Cox, 1970) was used to compare the tumor incidence of a control group with that of a group of dosed animals at each level. When results for two dosed groups are compared simultaneously with those for a control group, a correction to ensure an overall significance level of 0.05 is made. The Bonferroni inequality criterion (Miller, 1966) requires that the P value for any comparison be less than or equal to 0.025. When this correction was used, it is discussed in the narrative section. It is not presented in the tables, where the Fisher exact P values are shown.

The Cochran-Armitage test for linear trend in proportions, with continuity correction (Armitage, 1971), was also used. Under the assumption of a linear trend, this test determines if the slope of the dose-response curve is different from zero at the one-tailed 0.05 level of significance. Unless otherwise noted, the direction of the significant trend is a positive dose relationship. This method also provides a two-tailed test of departure from linear trend.

A time-adjusted analysis was applied. In this analysis, early deaths were excluded by basing the statistical tests on animals that survived until the appearance of the first tumor. Once this reduced set of data was obtained, the standard procedures for analyses of the incidence of tumors (Fisher exact tests, Cochran-Armitage tests, etc.) were followed.

Life table methods were used to analyze the incidence of tumors. Curves of the proportions surviving without an observed tumor were computed as in Saffiotti et al. (1972). The week during which an animal died naturally or was killed was entered as the time point of tumor observation. The methods of Cox and of Tarone were used for the statistical tests of the groups. The statistical tests were one-tailed.

III. RESULTS - RATS

A. Body Weights and Clinical Signs (Rats)

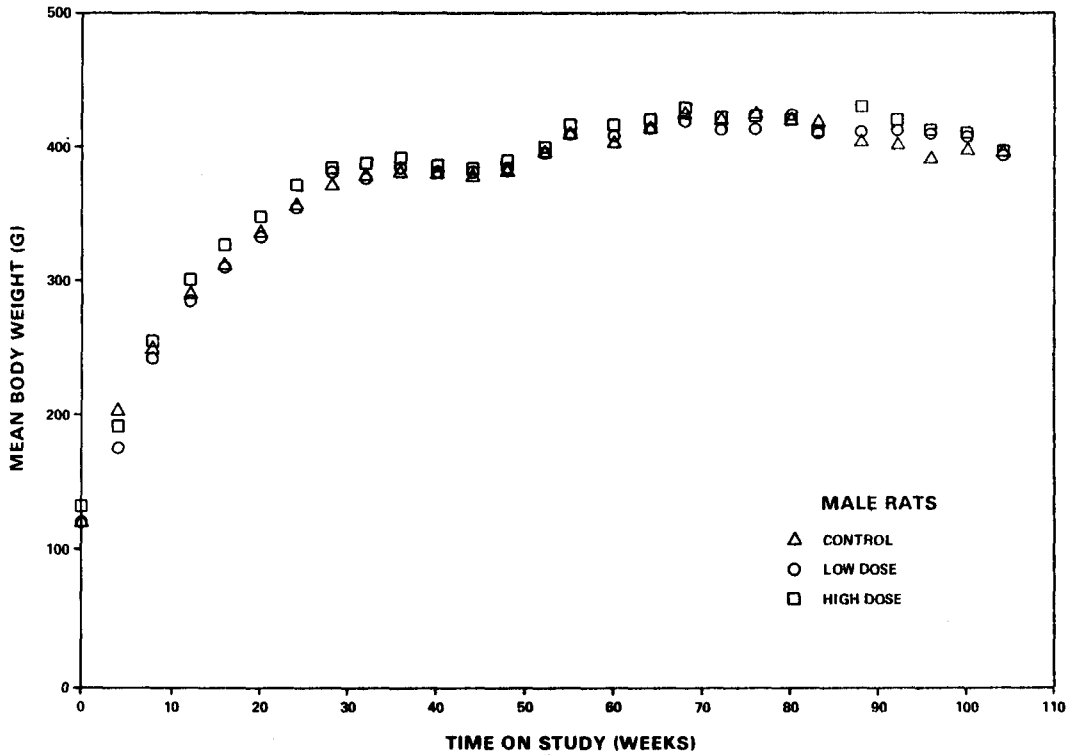
Mean body weights of dosed and control rats of either sex were comparable throughout the study (Figure 1 and Table 7). Clinical signs of dosed and control groups were comparable.

Feed consumption by low- and high-dose female rats was 87% and 79%, respectively, that of the controls. Feed consumption by low- and high-dose male rats was 92% and 95% that of the controls (Appendix F).

B. Survival (Rats)

Estimates of the probabilities of survival of male and female rats fed diets containing tara gum at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 2. No significant differences in survival were observed among dosed or control males or among dosed or control females.

In male rats, 33/50 (66%) of the controls, 33/50 (66%) of the low-dose, and 37/50 (74%) of the high-dose group lived to the end of the study at 105-107 weeks. In female rats, 36/50 (72%) of the controls, 40/50 (80%) of the low-dose, and 35/50 (70%) of the high-dose group lived to the end of the study at 106 weeks.



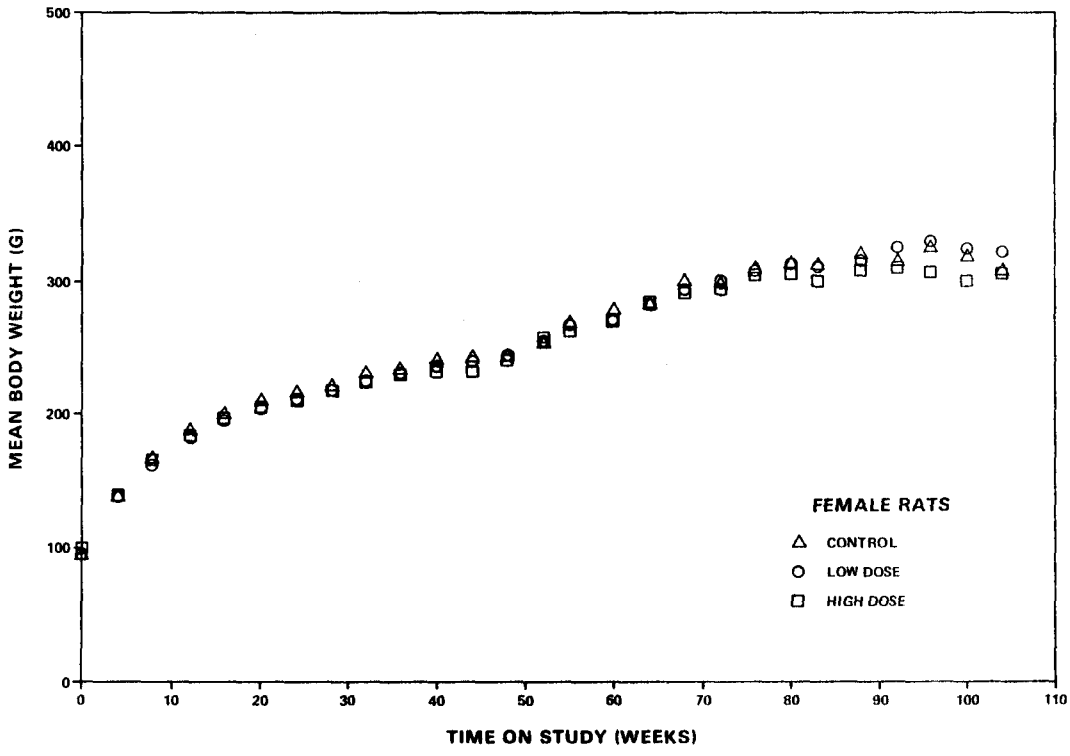


Figure 1. Growth Curves for Rats Fed Diets Containing Tara Gum

Table 7. Mean Body Weight Change (Relative to Controls) of Rats Fed Diets Containing Tara Gum

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls (%) (b)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Male rats	0	120(b)	119(b)	132(b)		
	24	236	235	238	0	+ 1
	44	257	260	251	+ 1	- 2
	64	296	296	290	0	- 2
	83	300	292	281	- 3	- 6
	104	276	275	264	0	- 4
Female rats	0	95(b)	95(b)	98(b)		
	24	121	117	113	- 3	- 7
	44	148	143	135	- 3	- 9
	64	189	188	187	- 1	- 1
	83	219	217	205	- 1	- 6
	104	214	227	209	+ 6	- 2

(a) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)} \times 100}{\text{Weight Change (Control Group)}}$$

(b) Initial weight

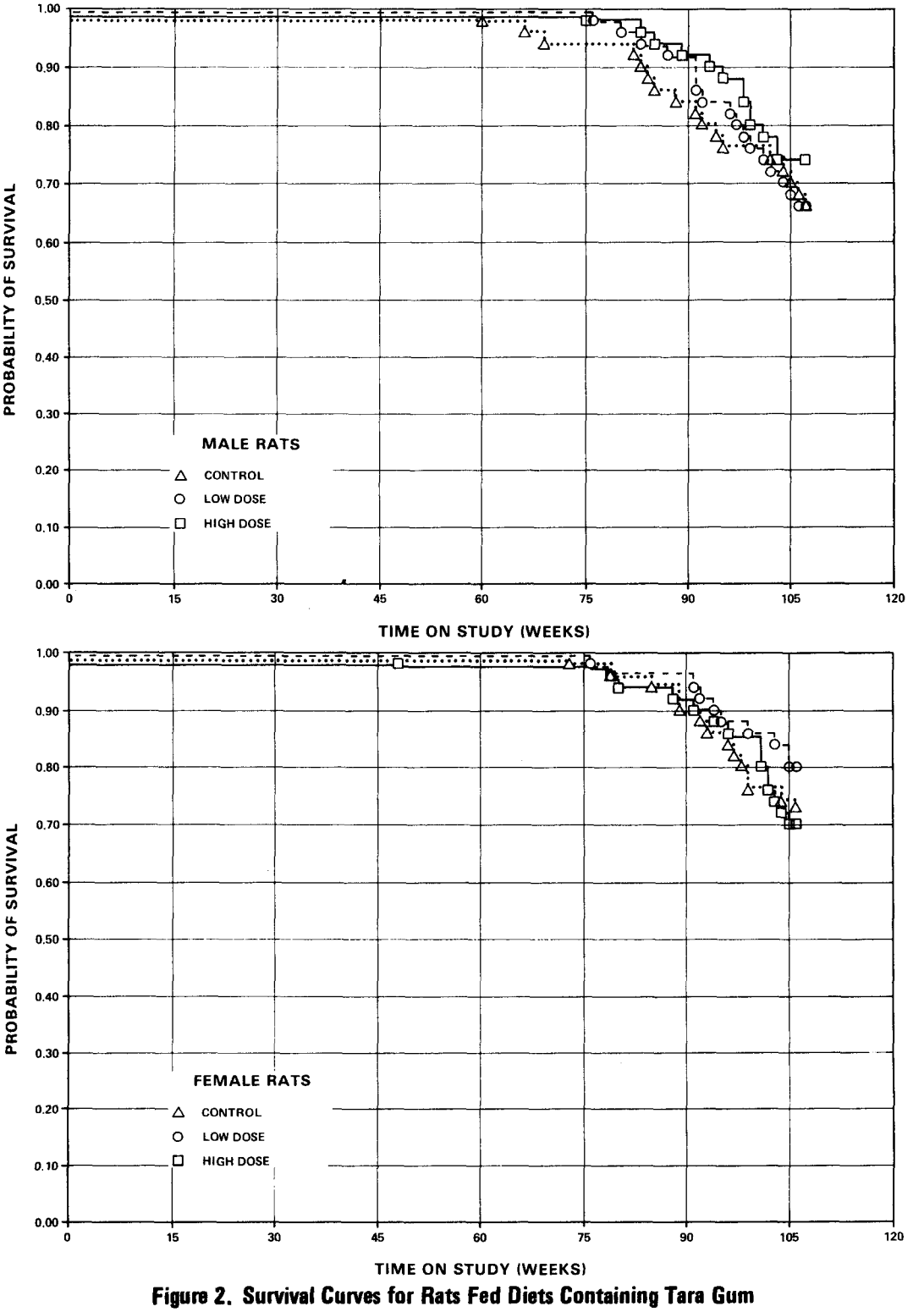


Figure 2. Survival Curves for Rats Fed Diets Containing Tara Gum

C. Pathology (Rats)

Histopathologic findings on neoplasms in rats are summarized in Appendix A, Tables A1 and A2; findings on nonneoplastic lesions are summarized in Appendix C, Tables C1 and C2.

A variety of neoplasms occurred in both control and dosed rats. A hemangiopericytoma (an unusual tumor) had metastasized to the lung in a control female rat. None of the neoplasms appeared to be related to the feeding of tara gum.

Many nonneoplastic lesions were found in control and dosed rats, but none were considered to be compound related.

D. Statistical Analyses of Results (Rats)

Tables 8 and 9 contain the statistical analyses of those primary tumors that satisfied both of the following criteria: (1) the tumor incidence was at least 5% in one of the three experimental groups and (2) the tumors occurred in at least two animals from one group.

Interstitial-cell tumors of the testis in male rats were observed in a statistically significant positive relation in the dosed groups compared with the control group (40/48, 83% in the controls; 46/46, 100% in the low-dose; and 48/48, 100% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the positive direction (P=0.001). The Fisher exact test between the control group and either of the dosed groups was significant (P=0.003 in the high-dose and P=0.003 in the low-dose groups). However, when time-adjusted analyses were applied to these data, the significance of the high-dose and low-dose effects was reduced (P=0.024 and P=0.026, respectively). There is a high spontaneous incidence of this tumor in F344 rats. For example, in all other chronic NCI bioassays initiated at this laboratory since 1977, the control incidence of interstitial-cell tumors of the testis in F344 male rats has been 84% (244/290), with a range of 72%-96%.

Islet-cell adenomas of the pancreatic islets in male rats were observed in decreased incidence in the dosed groups compared with the control group (5/45, 11% in the controls; 1/44, 2% in the low-dose; and 0/45, 0% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.011). The Fisher exact test between the high-dose group and the control group indicated a value of P=0.028. This value is above the value of P=0.025 required by the Bonferroni inequality criterion for an overall significance of P=0.05 when two dosed groups are compared with a common control group. In female rats, this tumor was not observed in a statistically significant proportion.

Life table tests, using the week during which an animal died naturally or was killed, did not materially alter the results reported in Tables 8 and 9.

The conclusion based on statistical analysis is that there is no site at which an increase in tumor incidence could be associated with the administration of the chemical.

Table 8. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Tara Gum (a)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	2/50(4)	3/50(6)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	1.500
Lower Limit		0.180	0.180
Upper Limit		17.329	17.329
Weeks to First Observed Tumor	107	106	105
Hematopoietic System: Myelomonocytic Leukemia (b)	14/50(28)	10/50(20)	14/50(28)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.714	1.000
Lower Limit		0.315	0.496
Upper Limit		1.558	2.018
Weeks to First Observed Tumor	66	91	85
Hematopoietic System: Leukemia (b)	14/50(28)	11/50(22)	16/50(32)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.786	1.143
Lower Limit		0.359	0.589
Upper Limit		1.674	2.243
Weeks to First Observed Tumor	66	87	83

Table 8. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Lymphoma or Leukemia (b)	15/50(30)	11/50(22)	16/50(32)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.733	1.067
Lower Limit		0.340	0.558
Upper Limit		1.532	2.050
Weeks to First Observed Tumor	66	87	83
Liver: Neoplastic Nodule (b)	1/49(2)	2/50(4)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.960	2.940
Lower Limit		0.106	0.246
Upper Limit		113.312	151.180
Weeks to First Observed Tumor	107	106	105
Pituitary: Adenoma, NOS (b)	13/43(30)	9/47(19)	11/45(24)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.633	0.809
Lower Limit		0.268	0.371
Upper Limit		1.435	1.736
Weeks to First Observed Tumor	66	101	98

Table 8. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Adrenal: Pheochromocytoma (b)	9/48(19)	15/48(31)	11/49(22)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.667	1.197
Lower Limit		0.761	0.497
Upper Limit		3.881	2.971
Weeks to First Observed Tumor	107	80	85
Thyroid: C-Cell Adenoma (b)	3/45(7)	2/44(5)	4/44(9)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.682	1.364
Lower Limit		0.059	0.245
Upper Limit		5.663	8.822
Weeks to First Observed Tumor	107	101	105
Thyroid: C-Cell Adenoma or Carcinoma (b)	4/45(9)	2/44(5)	4/44(9)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.511	1.023
Lower Limit		0.048	0.203
Upper Limit		3.371	5.160
Weeks to First Observed Tumor	107	101	105

Table 8. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Pancreatic Islets: Islet Cell Adenoma (b)	5/45(11)	1/44(2)	0/45(0)
P Values (c),(d)	P=0.011(N)	N.S.	P=0.028(N)
Relative Risk (Control) (e)		0.205	0.000
Lower Limit		0.004	0.000
Upper Limit		1.727	0.790
Weeks to First Observed Tumor	95	91	--
Preputial Gland: Adenoma, NOS (b)	6/50(12)	1/50(2)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.167	0.333
Lower Limit		0.004	0.034
Upper Limit		1.302	1.758
Weeks to First Observed Tumor	107	106	105
Preputial Gland: Adenoma, NOS or Carcinoma, NOS (b)	6/50(12)	2/50(4)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.333	0.333
Lower Limit		0.034	0.034
Upper Limit		1.758	1.758
Weeks to First Observed Tumor	107	106	105

Table 8. Analyses of the Incidence of Primary Tumors in Male Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Testis: Interstitial-Cell Tumor (b)	40/48(83)	46/46(100)	48/48(100)
P Values (c),(d)	P=0.001	P=0.003	P=0.003
Departure from Linear Trend (f)	P=0.041		
Relative Risk (Control) (e)		1.200	1.200
Lower Limit		1.050	1.053
Upper Limit		1.200	1.200
Weeks to First Observed Tumor	85	80	75

(a) Dosed groups received doses of 25,000 or 50,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicated a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.
(f) The probability level for departure from linear trend is given when P is less than 0.05 for any comparison.

Table 9. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Tara Gum (a)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	1/49(2)	2/50(4)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.960	2.940
Lower Limit		0.106	0.246
Upper Limit		113.312	151.180
Weeks to First Observed Tumor	106	106	106
Hematopoietic System: Myelomonocytic Leukemia (b)	6/50(12)	9/50(18)	7/50(14)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.500	1.167
Lower Limit		0.517	0.361
Upper Limit		4.749	3.911
Weeks to First Observed Tumor	89	92	80
Liver: Neoplastic Nodule (b)	2/49(4)	0/50(0)	1/49(2)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	0.500
Lower Limit		0.000	0.009
Upper Limit		3.313	9.284
Weeks to First Observed Tumor	97	--	103

Table 9. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Pituitary: Adenoma, NOS (b)	28/46(61)	29/44(66)	31/47(66)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.083	1.084
Lower Limit		0.766	0.773
Upper Limit		1.517	1.514
Weeks to First Observed Tumor	89	91	79
Adrenal: Pheochromocytoma (b)	2/49(4)	4/47(9)	0/50(0)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		2.085	0.000
Lower Limit		0.315	0.000
Upper Limit		22.172	3.313
Weeks to First Observed Tumor	106	106	--
Thyroid: C-Cell Adenoma (b)	3/46(7)	4/48(8)	3/47(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.278	0.979
Lower Limit		0.229	0.138
Upper Limit		8.300	6.958
Weeks to First Observed Tumor	106	106	106

Table 9. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Thyroid: C-Cell Adenoma or Carcinoma (b)	4/46(9)	6/48(13)	4/47(9)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.438	0.979
Lower Limit		0.366	0.193
Upper Limit		6.514	4.955
Weeks to First Observed Tumor	106	106	106
Pancreatic Islets: Islet-Cell Adenoma (b)	3/45(7)	0/47(0)	2/46(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.000	0.652
Lower Limit		0.000	0.057
Upper Limit		1.588	5.426
Weeks to First Observed Tumor	106	--	106
Mammary Gland: Fibroadenoma (b)	13/50(26)	21/50(42)	13/50(26)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.615	1.000
Lower Limit		0.876	0.477
Upper Limit		3.079	2.098
Weeks to First Observed Tumor	93	99	94

Table 9. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Mammary Gland: Adenoma NOS, or Adenocarcinoma, NOS(b)	1/50(2)	1/50(2)	3/50(6)
P Values (c), (d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.000	3.000
Lower Limit		0.013	0.251
Upper Limit		76.970	154.270
Weeks to First Observed Tumor	106	106	102
Clitoral Gland: Adenoma, NOS or Carcinoma, NOS (b)	3/50(6)	2/50(4)	2/50(4)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.667	0.667
Lower Limit		0.058	0.058
Upper Limit		5.570	5.570
Weeks to First Observed Tumor	106	105	105
Uterus: Endometrial Stromal Polyp (b)	6/47(13)	9/48(19)	7/49(14)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.469	1.119
Lower Limit		0.509	0.348
Upper Limit		4.631	3.742
Weeks to First Observed Tumor	73	106	105

Table 9. Analyses of the Incidence of Primary Tumors in Female Rats Fed Diets Containing Tara Gum (a)

(Continued)

(a) Dosed groups received doses of 25,000 or 50,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicated a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

IV. RESULTS - MICE

A. Body Weights and Clinical Signs (Mice)

Mean body weights of high-dose mice of either sex were lower than those of the controls from week 16 to the end of the study (Figure 3 and Table 10). Clinical signs of dosed and control mice were comparable. Feed consumption by dosed and control mice was comparable: low- and high-dose males, 100% and 102% of the controls; low- and high-dose females, 92% and 98% of controls (Appendix F).

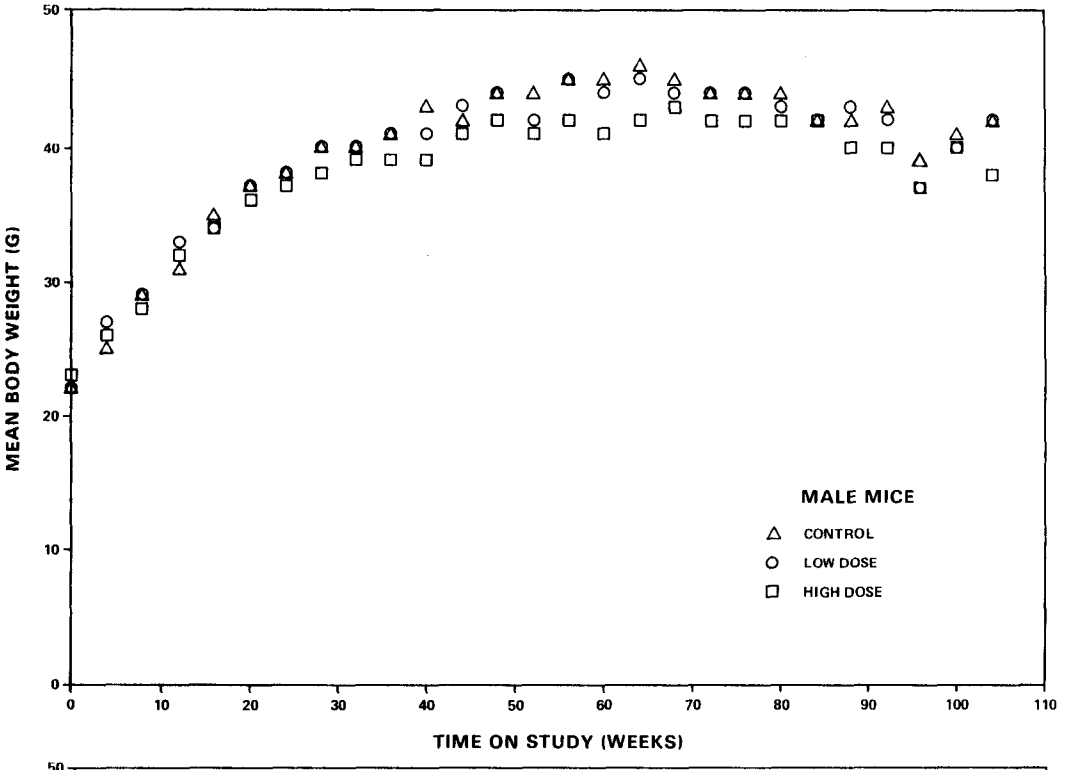
B. Survival (Mice)

Estimates of the probabilities of survival of male and female mice fed diets containing tara gum at the concentrations of this bioassay, together with those of the control group, are shown by the Kaplan and Meier curves in Figure 4. No significant differences in survival were observed between any of the groups of either sex.

In male mice, 42/50 (84%) of the controls, 39/50 (78%) of the low-dose, and 43/50 (86%) of the high-dose group lived to the end of the study at 105 weeks. In female mice, 33/50 (66%) of the controls, 36/50 (72%) of the low-dose, and 39/50, (78%) of the high-dose group lived to the end of the study at 105 weeks.

C. Pathology (Mice)

Histopathologic findings on neoplasms in mice are summararized in Appendix B, Tables B1 and B2; findings on nonneoplastic lesions are summarized in Appendix D, Tables D1 and D2.



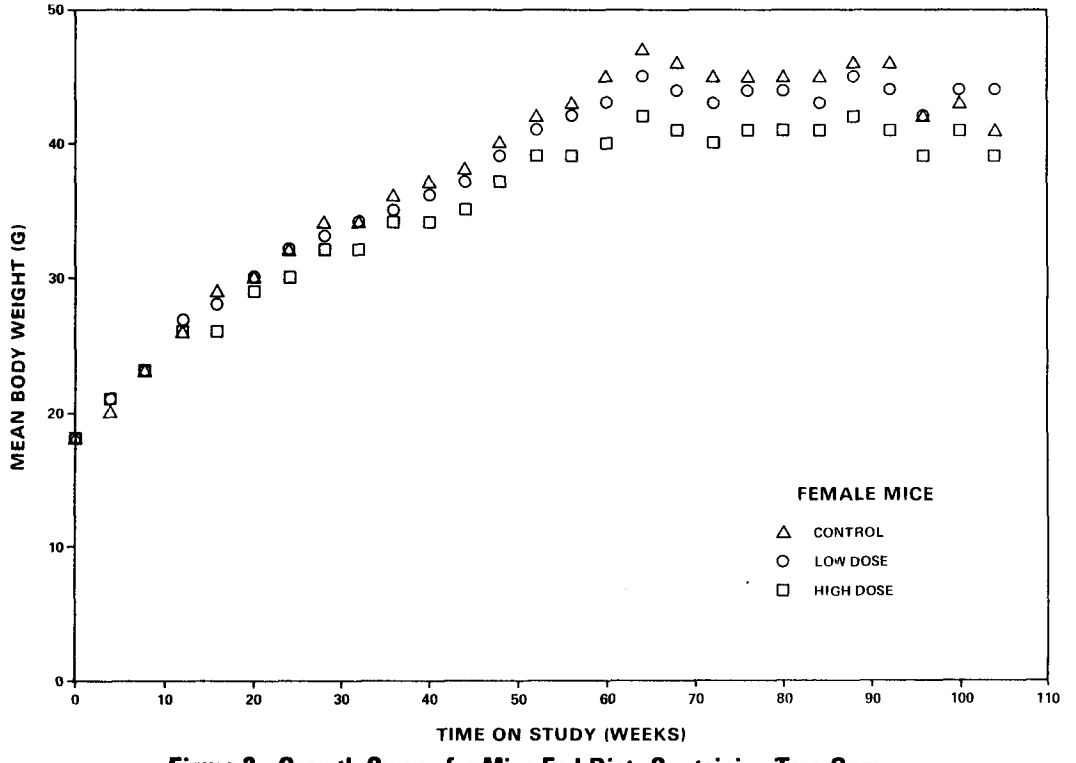


Figure 3. Growth Curves for Mice Fed Diets Containing Tara Gum

Table 10. Mean Body Weight Change (Relative to Controls) of Mice Fed Diets Containing Tara Gum

		Cumulative Mean Body Weight Change (grams)			Weight Change Relative to Controls (a)	
	Week No.	Control	Low Dose	High Dose	Low Dose	High Dose
Male mice	0	22(b)	22(b)	23(b)		
	24	16	16	14	0	-13
	44	20	21	18	+ 5	-10
	64	24	24	19	0	-20
	84	20	20	19	0	- 5
	104	20	20	15	0	-25
Female mice	0	18(b)	18(b)	18(b)		
	24	14	14	12	0	-14
	44	20	19	17	- 5	-15
	64	29	27	24	- 7	-17
	84	27	25	23	- 7	-15
	104	23	26	21	+11	- 9

(a) Weight Change Relative to Controls =

$$\frac{\text{Weight Change (Dosed Group)} - \text{Weight Change (Control Group)} \times 100}{\text{Weight Change (Control Group)}}$$

(b) Initial weight

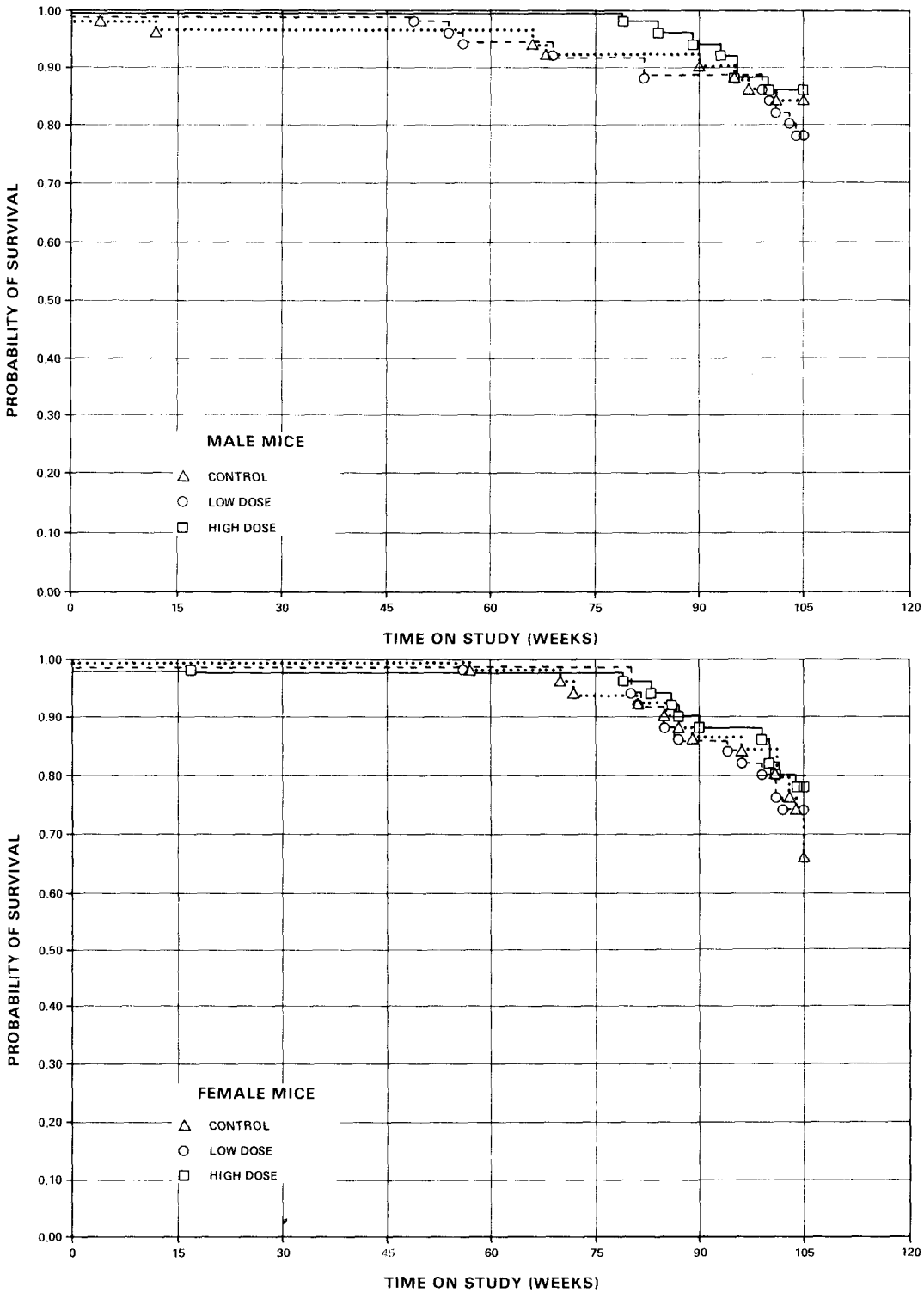


Figure 4. Survival Curves for Mice Fed Diets Containing Tara Gum

A variety of neoplasms and nonneoplastic lesions occurred in both control and dosed mice. None of the lesions appeared to be related to administration of tara gum.

D. Statistical Analyses of Results (Mice)

Tables 11 and 12 contain the statistical analyses of those primary tumors that satisfied both of the following criteria: (1) the tumor incidence was at least 5% in one of the three experimental groups and (2) the tumor occurred in at least two animals from one group.

Alveolar/bronchiolar adenomas or carcinomas in female mice were observed in decreased incidence in the dosed groups (8/50, 16% in the controls; 2/49, 4% in the low-dose; and 3/50, 6% in the high-dose). The Cochran-Armitage test for linear trend was not statistically significant. The Fisher exact test between the low-dose group and the controls was significant (P=0.049). This value is above the value of P=0.025 required by the Bonferroni inequality criterion for an overall significance of P=0.05 when two dosed groups are compared with a common control. In male mice, this tumor was not observed in a statistically significant proportion.

Hepatocellular adenomas or carcinomas in female mice were observed in a negative relation (10/49, 20% in the controls; 6/49, 12% in the low-dose; and 3/50, 6% in the high-dose). The Cochran-Armitage test for linear trend was statistically significant in the negative direction (P=0.023). The Fisher exact test between the high-dose group and the control group was significant (P=0.033). This value is above the P=0.025 probability level required for an overall significance rate of P=0.05 when multiple comparisons are made. No significant incidence was observed in the low-dose group; however, this tumor occurred in decreased incidence in the low-dose compared with the control group. In male mice, this tumor was not observed in statistically significant proportions.

Neither time-adjusted tests nor life table analyses materially changed the results reported in Tables 11 and 12.

The conclusion based on the statistical analysis of data is that there was no site at which an increase in tumor incidence could be associated with the administration of the chemical.

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Tara Gum (a)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	9/50(18)	11/50(22)	10/49(20)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.222	1.134
Lower Limit		0.506	0.454
Upper Limit		3.041	2.877
Weeks to First Observed Tumor	105	104	105
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	10/50(20)	11/50(22)	12/49(24)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.100	1.224
Lower Limit		0.467	0.536
Upper Limit		2.624	2.863
Weeks to First Observed Tumor	105	104	105
Hematopoietic System: Malignant Lymphoma, NOS (b)	5/50(10)	5/50(10)	6/50(12)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.000	1.200
Lower Limit		0.245	0.326
Upper Limit		4.082	4.660
Weeks to First Observed Tumor	97	82	93

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System: All Malignant Lymphoma (b)	6/50(12)	6/50(12)	6/50(12)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.000	1.000
Lower Limit		0.287	0.287
Upper Limit		3.489	3.489
Weeks to First Observed Tumor	97	82	93
Circulatory System: Hemangioma (b)	3/50(6)	3/50(6)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.000	1.000
Lower Limit		0.140	0.140
Upper Limit		7.133	7.133
Weeks to First Observed Tumor	105	99	105
Liver: Hepatocellular Adenoma (b)	8/50(16)	4/50(8)	4/50(8)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.500	0.500
Lower Limit		0.117	0.117
Upper Limit		1.737	1.737
Weeks to First Observed Tumor	105	101	84

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Liver: Hepatocellular Carcinoma (b)	9/50(18)	8/50(16)	14/50(28)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.889	1.556
Lower Limit		0.325	0.694
Upper Limit		2.382	3.688
Weeks to First Observed Tumor	90	99	79
Liver: Hepatocellular Adenoma or Carcinoma (b)	17/50(34)	12/50(24)	18/50(36)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.706	1.059
Lower Limit		0.346	0.587
Upper Limit		1.397	1.916
Weeks to First Observed Tumor	90	99	79
Harderian Gland: Adenoma, NOS (b)	4/50(8)	2/50(4)	3/50(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.500	0.750
Lower Limit		0.047	0.115
Upper Limit		3.318	4.206
Weeks to First Observed Tumor	105	105	105

Table 11. Analyses of the Incidence of Primary Tumors in Male Mice Fed Diets Containing Tara Gum (a)

(Continued)

(a) Dosed groups received doses of 25,000 or 50,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicated a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Tara Gum (a)

Topography: Morphology	Control	Low Dose	High Dose
Lung: Alveolar/Bronchiolar Adenoma (b)	7/50(14)	2/49(4)	2/50(4)
P Values (c),(d)	P=0.043(N)	N.S.	N.S.
Relative Risk (Control) (e)		0.292	0.286
Lower Limit		0.031	0.030
Upper Limit		1.439	1.411
Weeks to First Observed Tumor	105	105	105
Lung: Alveolar/Bronchiolar Adenoma or Carcinoma (b)	8/50(16)	2/49(4)	3/50(6)
P Values (c),(d)	N.S.	P=0.049(N)	N.S.
Relative Risk (Control) (e)		0.255	0.375
Lower Limit		0.027	0.067
Upper Limit		1.198	1.460
Weeks to First Observed Tumor	105	105	105
Hematopoietic System: Malignant Lymphoma, NOS (b)	16/50(32)	8/49(16)	13/50(26)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.510	0.813
Lower Limit		0.209	0.404
Upper Limit		1.139	1.603
Weeks to First Observed Tumor	70	96	79

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Hematopoietic System:			
Lymphoma (b)	16/50(32)	9/49(18)	13/50(26)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.574	0.813
Lower Limit		0.248	0.404
Upper Limit		1.239	1.603
Weeks to First Observed Tumor	70	96	79
Liver: Hepatocellular Adenoma (b)	9/49(18)	4/49(8)	1/50(2)
P Values (c),(d)	P=0.005(N)	N.S.	P=0.007(N)
Relative Risk (Control) (e)		0.444	0.109
Lower Limit		0.107	0.003
Upper Limit		1.476	0.740
Weeks to First Observed Tumor	104	105	105
Liver: Hepatocellular Adenoma or Carcinoma (b)	10/49(20)	6/49(12)	3/50(6)
P Values (c),(d)	P=0.023(N)	N.S.	P=0.033(N)
Relative Risk (Control) (e)		0.600	0.294
Lower Limit		0.194	0.055
Upper Limit		1.673	1.061
Weeks to First Observed Tumor	104	105	104

Table 12. Analyses of the Incidence of Primary Tumors in Female Mice Fed Diets Containing Tara Gum (a)

(Continued)

Topography: Morphology	Control	Low Dose	High Dose
Pituitary: Adenoma, NOS (b)	11/41(27)	10/36(28)	8/39(21)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		1.035	0.765
Lower Limit		0.447	0.299
Upper Limit		2.349	1.855
Weeks to First Observed Tumor	101	96	105
Adrenal: Adenoma, NOS (b)	1/46(2)	1/48(2)	3/48(6)
P Values (c),(d)	N.S.	N.S.	N.S.
Relative Risk (Control) (e)		0.958	2.875
Lower Limit		0.012	0.241
Upper Limit		73.689	147.682
Weeks to First Observed Tumor	103	105	104

(a) Dosed groups received doses of 25,000 or 50,000 ppm in the diet.
(b) Number of tumor-bearing animals/number of animals examined at site (percent).
(c) Beneath the incidence of tumors in the control group is the probability level for the Cochran-Armitage test when P is less than 0.05; otherwise, not significant (N.S.) is indicated. Beneath the incidence of tumors in a dosed group is the probability level for the Fisher exact test for the comparison of that dosed group with the control group when P is less than 0.05; otherwise, not significant (N.S.) is indicated.
(d) A negative trend (N) indicated a lower incidence in a dosed group than in a control group.
(e) The 95 percent confidence interval of the relative risk between each dosed group and the control group.

V. DISCUSSION

In the subchronic study, a decreased number of mature spermatozoa were observed in 4/10 male rats fed 50,000 ppm of the test chemical compared with 0/10 in controls. No other compound-related effects were observed in either rats or mice. Since measurement of relative organ weights was not a specified part of the subchronic study, previous findings of increased relative weights of the thyroid, cecum, and kidney in rats fed diets containing 50,000 ppm tara gum for 90 days (Til et al., 1975) were not confirmed in the current chronic study.

Mean body weights of dosed and control rats of either sex were comparable throughout the 2-year study. Mean body weights of high-dose mice of either sex were slightly lower than those of the controls from week 16 to the end of the study. The slight decrement in weight gain occurred in a dose-related fashion in both male and female mice. Feed consumption by dosed male rats and mice of either sex was similar to that of control animals. Low- and high-dose female rats ate 87% and 79% that of the controls.

Interstitial tumors of the testes occurred at incidences significantly higher in dosed male rats than those in the controls; however, F344 rats have a high spontaneous incidence rate of this tumor. Because of the variable historical incidence of this tumor in control male F344 rats and the marginal statistical significance when time-adjusted analyses are applied, the association between the increased incidence of this tumor and administration of tara gum is not established.

No other tumors were observed in either species at increased incidences that could be related to the oral administration of tara gum.

A significant negative trend in the incidence of pancreatic islet cell adenomas was observed in male rats. Likewise, significant negative trends were found in the proportions of female mice with alveolar/bronchiolar adenomas and with hepatocellular adenomas.

Two other galactomannan, legume-derived gums (guar gum, NTP, 1982a; locust bean gum, NTP 1982b) were tested at the laboratory used in the present study. Besides these, two additional gums have been tested recently by the NTP bioassay program (agar, NTP, 1982c; gum arabic, NTP, 1982d). Each of the four gums was added to the diet (2.5% and 5.0%) and fed for 104 weeks to F344 rats and B6C3F1 mice of both sexes. Under these test conditions all were considered to be not carcinogenic.

VI. CONCLUSIONS

Under the conditions of this bioassay, tara gum was not carcinogenic for F344 rats or B6C3F1 mice of either sex.

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APPENDIX A

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN RATS FED DIETS CONTAINING TARA GUM

TABLE A1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE RATS FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)	1 (2%)	
SQUAMOUS CELL CA. INSITU	1 (2%)		
SQUAMOUS CELL CARCINOMA	2 (4%)	1 (2%)	
BASAL-CELL CARCINOMA	1 (2%)		2 (4%)
SEBACEOUS ADENOMA		1 (2%)	
SARCOMA, NOS			1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS	1 (2%)	1 (2%)	1 (2%)
FIBROMA	1 (2%)	2 (4%)	2 (4%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(50)
ALVEOLAR/BRONCHIOLAR ADENOMA	2 (4%)	3 (6%)	3 (6%)
CORTICAL CARCINOMA, METASTATIC	1 (2%)		
OSTEOSARCOMA, METASTATIC			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
LEUKEMIA,NOS		1 (2%)	2 (4%)
MYELOMONOCYTIC LEUKEMIA	13 (26%)	10 (20%)	14 (28%)
*HEMATOPOIETIC SYSTEM	(50)	(50)	(50)
NEOPLASM, NOS		2 (4%)	1 (2%)
#SPLEEN	(47)	(49)	(48)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
#LYMPH NODE	(47)	(48)	(46)
CORTICAL CARCINOMA, METASTATIC	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#LIVER	(49)	(50)	(50)
MYELOMONOCYTIC LEUKEMIA	1 (2%)		
CIRCULATORY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
ANGIOSARCOMA	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(49)	(50)	(50)
NEOPLASTIC NODULE	1 (2%)	2 (4%)	3 (6%)
MESOTHELIOMA, METASTATIC	1 (2%)		
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
TUBULAR-CELL ADENOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(47)	(45)
ADENOMA, NOS	13 (30%)	9 (19%)	11 (24%)
#ADRENAL	(48)	(48)	(49)
CORTICAL CARCINOMA	1 (2%)		
PHEOCHROMOCYTOMA	9 (19%)	15 (31%)	11 (22%)
#THYROID	(45)	(44)	(44)
FOLLICULAR-CELL ADENOMA		1 (2%)	
C-CELL ADENOMA	3 (7%)	2 (5%)	4 (9%)
C-CELL CARCINOMA	1 (2%)		
#PANCREATIC ISLETS	(45)	(44)	(45)
ISLET-CELL ADENOMA	5 (11%)	1 (2%)	
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
FIBROADENOMA	2 (4%)	1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
*PREPUTIAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS		1 (2%)	
ADENOMA, NOS	6 (12%)	1 (2%)	2 (4%)
#TESTIS	(48)	(46)	(48)
INTERSTITIAL-CELL TUMOR	40 (83%)	46 (100%)	48 (100%)
NERVOUS SYSTEM			
#BRAIN	(50)	(48)	(50)
ASTROCYTOMA	1 (2%)		1 (2%)
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
OSTEOSARCOMA			1 (2%)
*SKULL	(50)	(50)	(50)
OSTEOMA		1 (2%)	
BODY CAVITIES			
*TUNICA VAGINALIS	(50)	(50)	(50)
MESOTHELIOMA, NOS	1 (2%)	1 (2%)	1 (2%)
MESOTHELIOMA, MALIGNANT	1 (2%)		
ALL OTHER SYSTEMS			
SITE UNKNOWN			
NEOPLASM, NOS	1		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A1. MALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	11	14	11
MORIBUND SACRIFICE	6	3	2
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	33	33	37
ANIMAL MISSING			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	45	49	49
TOTAL PRIMARY TUMORS	110	103	110
TOTAL ANIMALS WITH BENIGN TUMORS	45	47	49
TOTAL BENIGN TUMORS	82	84	83
TOTAL ANIMALS WITH MALIGNANT TUMORS	22	14	21
TOTAL MALIGNANT TUMORS	25	14	22
TOTAL ANIMALS WITH SECONDARY TUMORS#	2		1
TOTAL SECONDARY TUMORS	3		1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	3	5	5
TOTAL UNCERTAIN TUMORS	3	5	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

@ INCLUDES AUTOLYZED ANIMALS

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE A2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE RATS FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
SQUAMOUS CELL PAPILLOMA	1 (2%)		
*SUBCUT TISSUE	(50)	(50)	(50)
NEOPLASM, NOS		1 (2%)	
SARCOMA, NOS		1 (2%)	
FIBROMA	2 (4%)		2 (4%)
OSTEOSARCOMA, INVASIVE	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(50)
CARCINOMA, NOS, METASTATIC		1 (2%)	
SQUAMOUS CELL CARCINOMA			1 (2%)
ALVEOLAR/BRONCHIOLAR ADENOMA	1 (2%)	2 (4%)	2 (4%)
ALVEOLAR/BRONCHIOLAR CARCINOMA			1 (2%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MYELOMONOCYTIC LEUKEMIA	6 (12%)	9 (18%)	6 (12%)
*HEMATOPOIETIC SYSTEM	(50)	(50)	(50)
NEOPLASM, NOS	1 (2%)	1 (2%)	1 (2%)
#LIVER	(49)	(50)	(49)
MYELOMONOCYTIC LEUKEMIA			1 (2%)
#THYMUS	(35)	(41)	(32)
THYMOMA		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
CIRCULATORY SYSTEM			
*PLEURAL CAVITY	(50)	(50)	(50)
HEMANGIOPERICYTOMA, MALIGNANT	1 (2%)		
#LUNG	(49)	(50)	(50)
HEMANGIOPERICYTOMA, METASTATIC	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(49)	(50)	(49)
NEOPLASTIC NODULE	2 (4%)		1 (2%)
#STOMACH	(48)	(47)	(49)
SQUAMOUS CELL PAPILLOMA	2 (4%)		
URINARY SYSTEM			
#URINARY BLADDER	(45)	(46)	(48)
TRANSITIONAL-CELL CARCINOMA			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(44)	(47)
NEOPLASM, NOS	1 (2%)	1 (2%)	2 (4%)
ADENOMA, NOS	28 (61%)	29 (66%)	31 (66%)
#ADRENAL	(49)	(47)	(50)
CORTICAL ADENOMA		1 (2%)	1 (2%)
PHEOCHROMOCYTOMA	2 (4%)	4 (9%)	
#THYROID	(46)	(48)	(47)
FOLLICULAR-CELL CARCINOMA			1 (2%)
C-CELL ADENOMA	3 (7%)	4 (8%)	3 (6%)
C-CELL TUMOR	1 (2%)		
C-CELL CARCINOMA	1 (2%)	2 (4%)	1 (2%)
#PARATHYROID	(23)	(19)	(19)
ADENOMA, NOS		1 (5%)	
#PANCREATIC ISLETS	(45)	(47)	(46)
ISLET-CELL ADENOMA	3 (7%)		2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)	1 (2%)	2 (4%)
ADENOCARCINOMA, NOS			1 (2%)
FIBROADENOMA	13 (26%)	21 (42%)	13 (26%)
*CLITORAL GLAND	(50)	(50)	(50)
CARCINOMA,NOS	1 (2%)		
ADENOMA, NOS	2 (4%)	2 (4%)	2 (4%)
*VAGINA	(50)	(50)	(50)
LEIOMYOSARCOMA			1 (2%)
#UTERUS	(47)	(48)	(49)
ADENOCARCINOMA, NOS		1 (2%)	
SARCOMA, NOS		1 (2%)	1 (2%)
ENDOMETRIAL STROMAL POLYP	6 (13%)	9 (19%)	7 (14%)
#CERVIX UTERI	(47)	(48)	(49)
FIBROMA		1 (2%)	
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*ZYMBAL'S GLAND	(50)	(50)	(50)
CARCINOMA,NOS		1 (2%)	
MUSCULOSKELETAL SYSTEM			
*BONE	(50)	(50)	(50)
OSTEOSARCOMA		1 (2%)	
BODY CAVITIES			
NONE			

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE A2. FEMALE RATS: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(50)	(50)
MESOTHELIOMA, NOS			1 (2%)
OSTEOSARCOMA, METASTATIC	1 (2%)		
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHa	11	8	11
MORIBUND SACRIFICE	3	2	4
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	36	40	35
ANIMAL MISSING			
a INCLUDES AUTOLYZED ANIMALS			
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	40	48	47
TOTAL PRIMARY TUMORS	78	95	85
TOTAL ANIMALS WITH BENIGN TUMORS	35	43	40
TOTAL BENIGN TUMORS	64	76	65
TOTAL ANIMALS WITH MALIGNANT TUMORS	9	16	15
TOTAL MALIGNANT TUMORS	9	16	15
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	1	
TOTAL SECONDARY TUMORS	3	1	
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT	4	2	5
TOTAL UNCERTAIN TUMORS	5	3	5
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

APPENDIX B

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MICE FED DIETS CONTAINING TARA GUM

TABLE B1.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN MALE MICE FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(50)	(50)
SARCOMA, NOS		2 (4%)	1 (2%)
RESPIRATORY SYSTEM			
#LUNG	(50)	(50)	(49)
HEPATOCELLULAR CARCINOMA, METAST	2 (4%)	2 (4%)	
ALVEOLAR/BRONCHIOLAR ADENOMA	9 (18%)	11 (22%)	10 (20%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		2 (4%)
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(50)	(50)
MALIGNANT LYMPHOMA, NOS	4 (8%)	2 (4%)	4 (8%)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE	1 (2%)		
#SPLEEN	(49)	(49)	(48)
MALIGNANT LYMPHOMA, NOS	1 (2%)	2 (4%)	1 (2%)
#LYMPH NODE	(45)	(50)	(43)
MALIGNANT LYMPHOMA, NOS		1 (2%)	1 (2%)
#LIVER	(50)	(50)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	
CIRCULATORY SYSTEM			
#SPLEEN	(49)	(49)	(48)
HEMANGIOMA	1 (2%)		
ANGIOSARCOMA		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#LYMPH NODE	(45)	(50)	(43)
HEMANGIOMA	2 (4%)	3 (6%)	3 (7%)
ANGIOSARCOMA	1 (2%)		
#LIVER	(50)	(50)	(50)
ANGIOSARCOMA		1 (2%)	
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(49)	(47)	(48)
HEPATOCELLULAR CARCINOMA, METAST			1 (2%)
#LIVER	(50)	(50)	(50)
HEPATOCELLULAR ADENOMA	8 (16%)	4 (8%)	4 (8%)
HEPATOCELLULAR CARCINOMA	9 (18%)	8 (16%)	14 (28%)
#DUODENUM	(46)	(49)	(47)
ADENOMATOUS POLYP, NOS	1 (2%)		
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(42)	(43)	(39)
ADENOMA, NOS	2 (5%)	1 (2%)	1 (3%)
#ADRENAL	(47)	(50)	(48)
ADENOMA, NOS		2 (4%)	1 (2%)
CORTICAL ADENOMA	1 (2%)	1 (2%)	
#THYROID	(47)	(46)	(48)
FOLLICULAR-CELL ADENOMA			1 (2%)
#PANCREATIC ISLETS	(47)	(49)	(47)
ISLET-CELL ADENOMA	1 (2%)		1 (2%)
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(50)	(50)
ADENOMA, NOS	1 (2%)	1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
ADENOMA, NOS	4 (8%)	2 (4%)	3 (6%)
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
NONE			
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATH@	7	9	7
MORIBUND SACRIFICE	1	2	
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	42	39	43
ANIMAL MISSING			

@ INCLUDES AUTOLYZED ANIMALS

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B1. MALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	31	28	36
TOTAL PRIMARY TUMORS	47	43	48
TOTAL ANIMALS WITH BENIGN TUMORS	22	19	23
TOTAL BENIGN TUMORS	30	25	25
TOTAL ANIMALS WITH MALIGNANT TUMORS	16	15	19
TOTAL MALIGNANT TUMORS	17	18	23
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	2	1
TOTAL SECONDARY TUMORS	2	2	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT			
TOTAL UNCERTAIN TUMORS			
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
\# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

TABLE B2.

SUMMARY OF THE INCIDENCE OF NEOPLASMS IN FEMALE MICE FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING		1	
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(50)
SQUAMOUS CELL CARCINOMA	1 (2%)		
MALIGNANT MELANOMA			1 (2%)
SARCOMA, NOS		2 (4%)	1 (2%)
OSTEOSARCOMA		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(50)	(49)	(50)
CARCINOMA, NOS, METASTATIC			1 (2%)
HEPATOCELLULAR CARCINOMA, METAST	1 (2%)		
ALVEOLAR/BRONCHIOLAR ADENOMA	7 (14%)	2 (4%)	2 (4%)
ALVEOLAR/BRONCHIOLAR CARCINOMA	1 (2%)		1 (2%)
OSTEOSARCOMA, METASTATIC		1 (2%)	
HEMATOPOIETIC SYSTEM			
*MULTIPLE ORGANS	(50)	(49)	(50)
MALIGNANT LYMPHOMA, NOS	15 (30%)	7 (14%)	12 (24%)
*HEMATOPOIETIC SYSTEM	(50)	(49)	(50)
NEOPLASM, NOS		2 (4%)	
#SPLEEN	(50)	(45)	(50)
MALIGNANT LYMPHOMA, NOS			1 (2%)
#LYMPH NODE	(46)	(45)	(46)
MALIGNANT LYMPHOMA, NOS		1 (2%)	
#LIVER	(49)	(49)	(50)
MALIG.LYMPHOMA, HISTIOCYTIC TYPE		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#PEYER'S PATCH	(46)	(42)	(49)
MALIGNANT LYMPHOMA, NOS	1 (2%)		
CIRCULATORY SYSTEM			
#SPLEEN	(50)	(45)	(50)
ANGIOSARCOMA		1 (2%)	
#LIVER	(49)	(49)	(50)
HEMANGIOMA	1 (2%)		
ANGIOSARCOMA	1 (2%)		1 (2%)
DIGESTIVE SYSTEM			
#SALIVARY GLAND	(46)	(46)	(50)
CARCINOMA, NOS, INVASIVE			1 (2%)
#LIVER	(49)	(49)	(50)
HEPATOCELLULAR ADENOMA	9 (18%)	4 (8%)	1 (2%)
HEPATOCELLULAR CARCINOMA	1 (2%)	2 (4%)	2 (4%)
#STOMACH	(48)	(45)	(49)
SQUAMOUS CELL PAPILLOMA			1 (2%)
URINARY SYSTEM			
NONE			
ENDOCRINE SYSTEM			
#PITUITARY	(41)	(36)	(39)
ADENOMA, NOS	11 (27%)	10 (28%)	8 (21%)
#ADRENAL	(46)	(48)	(48)
ADENOMA, NOS	1 (2%)	1 (2%)	3 (6%)
PHEOCHROMOCYTOMA	1 (2%)		
#THYROID	(48)	(42)	(47)
FOLLICULAR-CELL ADENOMA	1 (2%)		
#PANCREATIC ISLETS	(46)	(42)	(47)
ISLET-CELL ADENOMA			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(49)	(50)
ADENOCARCINOMA, NOS	1 (2%)		
#UTERUS	(49)	(46)	(46)
NEOPLASM, NOS		1 (2%)	
SARCOMA, NOS	1 (2%)		
ENDOMETRIAL STROMAL SARCOMA	1 (2%)		
#OVARY	(43)	(36)	(44)
GRANULOSA-CELL TUMOR			1 (2%)
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(49)	(50)
CARCINOMA,NOS			1 (2%)
ADENOMA, NOS	1 (2%)	1 (2%)	
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
*MULTIPLE ORGANS	(50)	(49)	(50)
OSTEOSARCOMA, METASTATIC	1 (2%)		
LEG			
OSTEOSARCOMA	1		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE B2. FEMALE MICE: NEOPLASMS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ANIMAL DISPOSITION SUMMARY			
ANIMALS INITIALLY IN STUDY	50	50	50
NATURAL DEATHa	12	12	11
MORIBUND SACRIFICE	5	1	
SCHEDULED SACRIFICE			
ACCIDENTALLY KILLED			
TERMINAL SACRIFICE	33	36	39
ANIMAL MISSING		1	
TUMOR SUMMARY			
TOTAL ANIMALS WITH PRIMARY TUMORS*	34	26	26
TOTAL PRIMARY TUMORS	56	36	37
TOTAL ANIMALS WITH BENIGN TUMORS	24	14	14
TOTAL BENIGN TUMORS	32	18	16
TOTAL ANIMALS WITH MALIGNANT TUMORS	21	13	19
TOTAL MALIGNANT TUMORS	24	15	20
TOTAL ANIMALS WITH SECONDARY TUMORS#	2	1	1
TOTAL SECONDARY TUMORS	2	1	2
TOTAL ANIMALS WITH TUMORS UNCERTAIN-BENIGN OR MALIGNANT		3	1
TOTAL UNCERTAIN TUMORS		3	1
TOTAL ANIMALS WITH TUMORS UNCERTAIN-PRIMARY OR METASTATIC			
TOTAL UNCERTAIN TUMORS			

a INCLUDES AUTOLYZED ANIMALS

* PRIMARY TUMORS: ALL TUMORS EXCEPT SECONDARY TUMORS
# SECONDARY TUMORS: METASTATIC TUMORS OR TUMORS INVASIVE INTO AN ADJACENT ORGAN

APPENDIX C

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN RATS FED DIETS CONTAINING TARA GUM

TABLE C1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE RATS FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST		1 (2%)	1 (2%)
HEMORRHAGE		1 (2%)	
INFLAMMATION, NOS		1 (2%)	1 (2%)
HYPERPLASIA, BASAL CELL			1 (2%)
HYPERKERATOSIS		2 (4%)	1 (2%)
ACANTHOSIS	1 (2%)	1 (2%)	1 (2%)
*SUBCUT TISSUE	(50)	(50)	(50)
HEMORRHAGE	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG/BRONCHUS	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
INFLAMMATION, FOCAL			1 (2%)
#LUNG	(50)	(50)	(50)
HEMORRHAGE	2 (4%)	2 (4%)	
INFLAMMATION, NOS	4 (8%)		
PNEUMONIA, CHRONIC MURINE	1 (2%)	1 (2%)	1 (2%)
REACTION, FOREIGN BODY	1 (2%)		
HYPERPLASIA, ADENOMATOUS	1 (2%)		
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)		
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(48)	(48)	(50)
FIBROSIS		1 (2%)	
HYPOPLASIA, NOS		1 (2%)	
#SPLEEN	(47)	(49)	(48)
INFARCT, NOS		1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
HEMATOPOIESIS	11 (23%)	4 (8%)	
#LYMPH NODE	(47)	(48)	(46)
HEMORRHAGIC CYST		1 (2%)	
INFLAMMATION, NOS		1 (2%)	
ABSCESS, NOS		1 (2%)	
#LIVER	(49)	(50)	(50)
HEMATOPOIESIS		1 (2%)	
CIRCULATORY SYSTEM			
#HEART	(50)	(49)	(50)
THROMBOSIS, NOS	1 (2%)	1 (2%)	
THROMBUS, MURAL	1 (2%)		
INFLAMMATION, NOS		1 (2%)	
PERIARTERITIS			1 (2%)
PERIVASCULITIS	1 (2%)	1 (2%)	
#MYOCARDIUM	(50)	(49)	(50)
DEGENERATION, NOS	30 (60%)	25 (51%)	23 (46%)
*PANCREATIC ARTERY	(50)	(50)	(50)
PERIVASCULITIS	2 (4%)	1 (2%)	2 (4%)
DIGESTIVE SYSTEM			
#LIVER	(49)	(50)	(50)
DILATATION, NOS		1 (2%)	
FIBROSIS		1 (2%)	
DEGENERATION, CYSTIC		1 (2%)	
NECROSIS, NOS			1 (2%)
NECROSIS, FOCAL	7 (14%)	5 (10%)	2 (4%)
NECROSIS, FAT		1 (2%)	
INFARCT, NOS	1 (2%)		
METAMORPHOSIS FATTY	7 (14%)	7 (14%)	4 (8%)
BASOPHILIC CYTO CHANGE	14 (29%)	7 (14%)	13 (26%)
FOCAL CELLULAR CHANGE	8 (16%)	14 (28%)	12 (24%)
CLEAR-CELL CHANGE		1 (2%)	
#BILE DUCT	(49)	(50)	(50)
HYPERPLASIA, NOS		1 (2%)	
#PANCREATIC ACINUS	(45)	(44)	(45)
ATROPHY, NOS	2 (4%)	4 (9%)	2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#STOMACH	(48)	(48)	(48)
INFLAMMATION, NOS		2 (4%)	
ULCER, NOS		1 (2%)	
HYPERPLASIA, BASAL CELL	5 (10%)	2 (4%)	2 (4%)
HYPERKERATOSIS	1 (2%)	1 (2%)	1 (2%)
ACANTHOSIS	5 (10%)		
#GASTRIC MUCOSA	(48)	(48)	(48)
HYPERPLASIA, FOCAL			1 (2%)
#GASTRIC SUBMUCOSA	(48)	(48)	(48)
REACTION, FOREIGN BODY			1 (2%)
#FORESTOMACH	(48)	(48)	(48)
NECROSIS, NOS		1 (2%)	
#PEYER'S PATCH	(45)	(44)	(43)
HYPERPLASIA, NOS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
MINERALIZATION			2 (4%)
INFLAMMATION, NOS			1 (2%)
NEPHROPATHY	41 (82%)	41 (82%)	41 (82%)
#KIDNEY/TUBULE	(50)	(50)	(50)
NECROSIS, NOS	1 (2%)		
#KIDNEY/PELVIS	(50)	(50)	(50)
HYPERPLASIA, EPITHELIAL			2 (4%)
#URINARY BLADDER	(43)	(47)	(45)
INFLAMMATION, NOS			1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
*PROSTATIC URETHRA	(50)	(50)	(50)
INFLAMMATION, NOS			1 (2%)
HYPERPLASIA, EPITHELIAL			1 (2%)
ENDOCRINE SYSTEM			
#PITUITARY	(43)	(47)	(45)
DILATATION, NOS	1 (2%)	1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#ADRENAL	(48)	(48)	(49)
DILATATION, NOS	1 (2%)		
CALCIFICATION, NOS			1 (2%)
#ADRENAL CORTEX	(48)	(48)	(49)
METAMORPHOSIS FATTY			1 (2%)
HYPERTROPHY, NOS		1 (2%)	
HYPERTROPHY, FOCAL	1 (2%)		
#ADRENAL MEDULLA	(48)	(48)	(49)
HYPERPLASIA, NOS	11 (23%)	4 (8%)	3 (6%)
#THYROID	(45)	(44)	(44)
HYPERPLASIA, C-CELL	2 (4%)	2 (5%)	3 (7%)
HYPERPLASIA, FOLLICULAR-CELL		1 (2%)	
#PANCREATIC ISLETS	(45)	(44)	(45)
HYPERPLASIA, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	1 (2%)		
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, NOS	4 (8%)	2 (4%)	
NECROSIS, NOS	1 (2%)	1 (2%)	
#PROSTATE	(42)	(45)	(41)
INFLAMMATION, NOS	1 (2%)	3 (7%)	
#TESTIS	(48)	(46)	(48)
MINERALIZATION	1 (2%)	9 (20%)	9 (19%)
ATROPHY, NOS	4 (8%)	3 (7%)	1 (2%)
HYPERPLASIA, INTERSTITIAL CELL	3 (6%)		
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
HYPERPLASIA, FOCAL	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C1. MALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
MUSCULOSKELETAL SYSTEM			
*FASCIA	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
BODY CAVITIES			
*ABDOMINAL CAVITY	(50)	(50)	(50)
MINERALIZATION	1 (2%)		
NECROSIS, FAT	1 (2%)		1 (2%)
ALL OTHER SYSTEMS			
OMENTUM			
MINERALIZATION		1	
NECROSIS, FAT	5	6	2
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	2		
AUTO/NECROPSY/HISTO PERF	1	1	

\# NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE RATS FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
EPIDERMAL INCLUSION CYST	1 (2%)		
HYPERPLASIA, BASAL CELL		1 (2%)	
RESPIRATORY SYSTEM			
#LUNG	(49)	(50)	(50)
INFLAMMATION, NOS	1 (2%)	2 (4%)	
REACTION, FOREIGN BODY		2 (4%)	
HYPERPLASIA, ALVEOLAR EPITHELIUM	1 (2%)		
HEMATOPOIETIC SYSTEM			
#SPLEEN	(47)	(50)	(48)
MINERALIZATION	1 (2%)		
NECROSIS, NOS	1 (2%)		
FOCAL CELLULAR CHANGE		1 (2%)	
MASTOCYTOSIS	1 (2%)		
HEMATOPOIESIS	17 (36%)	24 (48%)	7 (15%)
#LYMPH NODE	(44)	(47)	(49)
PLASMACYTOSIS		1 (2%)	
HEMATOPOIESIS		1 (2%)	
#LIVER	(49)	(50)	(49)
MASTOCYTOSIS	1 (2%)		
HEMATOPOIESIS		1 (2%)	
CIRCULATORY SYSTEM			
#HEART	(48)	(50)	(50)
INFLAMMATION, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
PERIVASCULITIS		1 (2%)	1 (2%)
#MYOCARDIUM	(48)	(50)	(50)
DEGENERATION, NOS	10 (21%)	9 (18%)	5 (10%)
#ENDOCARDIUM	(48)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
#CARDIAC VALVE	(48)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
*PANCREATIC ARTERY	(50)	(50)	(50)
PERIVASCULITIS			1 (2%)
DIGESTIVE SYSTEM			
#LIVER	(49)	(50)	(49)
INFLAMMATION, NOS	1 (2%)		
FIBROSIS	2 (4%)	1 (2%)	
NECROSIS, FOCAL	3 (6%)	5 (10%)	
METAMORPHOSIS FATTY	6 (12%)	5 (10%)	4 (8%)
CALCIFICATION, FOCAL	1 (2%)		
BASOPHILIC CYTO CHANGE	31 (63%)	32 (64%)	32 (65%)
FOCAL CELLULAR CHANGE	4 (8%)	6 (12%)	3 (6%)
#PANCREATIC ACINUS	(45)	(47)	(46)
ATROPHY, NOS	1 (2%)		1 (2%)
HYPERTROPHY, FOCAL		1 (2%)	
#STOMACH	(48)	(47)	(49)
NECROSIS, NOS	1 (2%)		
HYPERPLASIA, BASAL CELL	5 (10%)	2 (4%)	
HYPERKERATOSIS		3 (6%)	
ACANTHOSIS	5 (10%)	2 (4%)	
#PEYER'S PATCH	(48)	(46)	(48)
HYPERPLASIA, NOS			1 (2%)
URINARY SYSTEM			
#KIDNEY	(49)	(50)	(49)
MINERALIZATION	4 (8%)	1 (2%)	6 (12%)
HYDRONEPHROSIS		1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, NOS	2 (4%)		
INFLAMMATION, INTERSTITIAL		1 (2%)	
NEPHROPATHY	32 (65%)	32 (64%)	24 (49%)
#KIDNEY/PELVIS	(49)	(50)	(49)
HYPERPLASIA, EPITHELIAL	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(46)	(44)	(47)
DILATATION, NOS	2 (4%)	1 (2%)	3 (6%)
#ADRENAL	(49)	(47)	(50)
DILATATION, NOS	1 (2%)		
HEMORRHAGE	1 (2%)		
METAMORPHOSIS FATTY		1 (2%)	
#ADRENAL CORTEX	(49)	(47)	(50)
HYPERTROPHY, FOCAL	3 (6%)		
#ADRENAL MEDULLA	(49)	(47)	(50)
HYPERPLASIA, NOS		2 (4%)	
#THYROID	(46)	(48)	(47)
HYPERPLASIA, C-CELL	5 (11%)	6 (13%)	6 (13%)
REPRODUCTIVE SYSTEM			
*MAMMARY GLAND	(50)	(50)	(50)
GALACTOCELE	8 (16%)	8 (16%)	11 (22%)
INFLAMMATION, NOS	1 (2%)		
HYPERPLASIA, NOS			1 (2%)
*CLITORAL GLAND	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	
METAPLASIA, SQUAMOUS		1 (2%)	
#UTERUS	(47)	(48)	(49)
HYDROMETRA	1 (2%)	1 (2%)	
INFLAMMATION, NOS			1 (2%)
HYPERPLASIA, ADENOMATOUS		2 (4%)	
#UTERUS/ENDOMETRIUM	(47)	(48)	(49)
HYPERPLASIA, NOS		1 (2%)	1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE C2. FEMALE RATS: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#OVARY	(47)	(48)	(48)
MINERALIZATION	1 (2%)		
NERVOUS SYSTEM			
NONE			
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
NONE			
ALL OTHER SYSTEMS			
OMENTUM			
NECROSIS, FAT		2	
SPECIAL MORPHOLOGY SUMMARY			
AUTO/NECROPSY/HISTO PERF	1	1	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX D

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MICE FED DIETS CONTAINING TARA GUM

TABLE D1.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN MALE MICE FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS NECROPSIED	50	50	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	50	50
INTEGUMENTARY SYSTEM			
*SKIN	(50)	(50)	(50)
INFLAMMATION, NOS		1 (2%)	2 (4%)
HYPERKERATOSIS		1 (2%)	
*SUBCUT TISSUE	(50)	(50)	(50)
ABSCESS, NOS		1 (2%)	
FIBROSIS	1 (2%)		
NECROSIS, NOS	1 (2%)		
RESPIRATORY SYSTEM			
#LUNG/BRONCHUS	(50)	(50)	(49)
INFLAMMATION, NOS	14 (28%)	16 (32%)	19 (39%)
#LUNG	(50)	(50)	(49)
MINERALIZATION	3 (6%)		2 (4%)
HEMORRHAGE	1 (2%)	1 (2%)	
INFLAMMATION, NOS	15 (30%)	18 (36%)	17 (35%)
INFLAMMATION, FOCAL		1 (2%)	3 (6%)
HEMATOPOIETIC SYSTEM			
#SPLEEN	(49)	(49)	(48)
HEMATOPOIESIS	13 (27%)	10 (20%)	3 (6%)
#LYMPH NODE	(45)	(50)	(43)
HEMORRHAGIC CYST			1 (2%)
ABSCESS, NOS			1 (2%)
HEMATOPOIESIS	13 (29%)	5 (10%)	10 (23%)
#LUMBAR LYMPH NODE	(45)	(50)	(43)
HEMORRHAGE	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#LIVER	(50)	(50)	(50)
HEMATOPOIESIS	1 (2%)	2 (4%)	3 (6%)
CIRCULATORY SYSTEM			
#HEART	(50)	(50)	(49)
MINERALIZATION			1 (2%)
ENDOCARDITIS, BACTERIAL		1 (2%)	
#MYOCARDIUM	(50)	(50)	(49)
DEGENERATION, NOS			1 (2%)
#STOMACH	(48)	(47)	(47)
PERIVASCULITIS		1 (2%)	
#KIDNEY	(50)	(50)	(50)
PERIVASCULITIS		1 (2%)	
DIGESTIVE SYSTEM			
#LIVER	(50)	(50)	(50)
ABSCESS, NOS			1 (2%)
FIBROSIS	1 (2%)		
NECROSIS, FOCAL	1 (2%)	1 (2%)	1 (2%)
NECROSIS, ISCHEMIC	1 (2%)		
METAMORPHOSIS FATTY	1 (2%)	3 (6%)	1 (2%)
CLEAR-CELL CHANGE	2 (4%)		
*GALLBLADDER	(50)	(50)	(50)
MINERALIZATION			1 (2%)
INFLAMMATION, NOS	1 (2%)		1 (2%)
NECROSIS, NOS			1 (2%)
POLYP	1 (2%)		
#PANCREATIC ACINUS	(47)	(49)	(47)
HYPERTROPHY, FOCAL		1 (2%)	
#STOMACH	(48)	(47)	(47)
INFLAMMATION, NOS	2 (4%)		2 (4%)
NECROSIS, NOS		1 (2%)	
HYPERPLASIA, BASAL CELL	1 (2%)	1 (2%)	1 (2%)
HYPERKERATOSIS	2 (4%)	2 (4%)	2 (4%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
ACANTHOSIS	1 (2%)	2 (4%)	1 (2%)
#GASTRIC MUCOSA	(48)	(47)	(47)
HYPERPLASIA, FOCAL		1 (2%)	
#PEYER'S PATCH	(46)	(49)	(47)
HYPERPLASIA, NOS		1 (2%)	
URINARY SYSTEM			
#KIDNEY	(50)	(50)	(50)
MINERALIZATION	17 (34%)	2 (4%)	1 (2%)
PYELONEPHRITIS, NOS	1 (2%)		
INFLAMMATION, NOS		3 (6%)	
NEPHROPATHY	3 (6%)	2 (4%)	6 (12%)
ENDOCRINE SYSTEM			
#ADRENAL	(47)	(50)	(48)
HYPERPLASIA, NOS	11 (23%)	6 (12%)	5 (10%)
#ADRENAL CORTEX	(47)	(50)	(48)
HYPERTROPHY, FOCAL	2 (4%)	2 (4%)	1 (2%)
REPRODUCTIVE SYSTEM			
*PREPUTIAL GLAND	(50)	(50)	(50)
INFLAMMATION, NOS	4 (8%)	2 (4%)	2 (4%)
ABSCESS, NOS	1 (2%)	1 (2%)	
HYPERPLASIA, NOS		1 (2%)	
#TESTIS	(50)	(49)	(50)
MINERALIZATION		1 (2%)	1 (2%)
ATROPHY, NOS		1 (2%)	1 (2%)
NERVOUS SYSTEM			
#BRAIN	(50)	(50)	(49)
GLIOSIS		1 (2%)	
NECROSIS, FOCAL		1 (2%)	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D1. MALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
SPECIAL SENSE ORGANS			
*HARDERIAN GLAND	(50)	(50)	(50)
INFLAMMATION, NOS	1 (2%)		
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*MESENTERY	(50)	(50)	(50)
INFLAMMATION, FOCAL GRANULOMATOU		1 (2%)	
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	3	7	3
AUTO/NECROPSY/HISTO PERF	2		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2.

SUMMARY OF THE INCIDENCE OF NONNEOPLASTIC LESIONS IN FEMALE MICE FED DIETS CONTAINING TARA GUM

	CONTROL	LOW DOSE	HIGH DOSE
ANIMALS INITIALLY IN STUDY	50	50	50
ANIMALS MISSING		1	
ANIMALS NECROPSIED	50	49	50
ANIMALS EXAMINED HISTOPATHOLOGICALLY	50	49	50
INTEGUMENTARY SYSTEM			
*SUBCUT TISSUE	(50)	(49)	(50)
INFLAMMATION, NOS	1 (2%)	1 (2%)	
RESPIRATORY SYSTEM			
#LUNG/BRONCHUS	(50)	(49)	(50)
INFLAMMATION, NOS	13 (26%)	17 (35%)	12 (24%)
#LUNG	(50)	(49)	(50)
MINERALIZATION	1 (2%)		
INFLAMMATION, NOS	15 (30%)	18 (37%)	14 (28%)
INFLAMMATION, FOCAL	2 (4%)	2 (4%)	2 (4%)
HEMATOPOIETIC SYSTEM			
#BONE MARROW	(46)	(44)	(43)
FIBROSIS		1 (2%)	
HYPERPLASIA, HEMATOPOIETIC		1 (2%)	
#SPLEEN	(50)	(45)	(50)
FIBROSIS	1 (2%)		
NECROSIS, NOS	1 (2%)		
HYPERPLASIA, NOS		1 (2%)	
HEMATOPOIESIS	25 (50%)	18 (40%)	19 (38%)
#LYMPH NODE	(46)	(45)	(46)
HEMORRHAGE	1 (2%)		
ABSCESS, NOS			1 (2%)
HEMATOPOIESIS	4 (9%)	2 (4%)	4 (9%)
#LIVER	(49)	(49)	(50)
HEMATOPOIESIS	7 (14%)	5 (10%)	8 (16%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
#ADRENAL	(46)	(48)	(48)
HEMATOPOIESIS			1 (2%)
CIRCULATORY SYSTEM			
#HEART	(50)	(49)	(50)
MINERALIZATION	1 (2%)		
DIGESTIVE SYSTEM			
#LIVER	(49)	(49)	(50)
NECROSIS, FOCAL	4 (8%)	3 (6%)	2 (4%)
NECROSIS, COAGULATIVE		1 (2%)	
METAMORPHOSIS FATTY	4 (8%)	4 (8%)	
EOSINOPHILIC CYTO CHANGE	1 (2%)		
CLEAR-CELL CHANGE		1 (2%)	2 (4%)
#PANCREAS	(46)	(42)	(47)
NECROSIS, NOS			1 (2%)
#PANCREATIC ACINUS	(46)	(42)	(47)
ATROPHY, NOS			1 (2%)
HYPERTROPHY, FOCAL		1 (2%)	
#STOMACH	(48)	(45)	(49)
DIVERTICULUM			1 (2%)
INFLAMMATION, NOS	1 (2%)	5 (11%)	8 (16%)
NECROSIS, NOS	2 (4%)	4 (9%)	2 (4%)
HYPERPLASIA, BASAL CELL	4 (8%)	4 (9%)	2 (4%)
HYPERKERATOSIS	14 (29%)	16 (36%)	16 (33%)
ACANTHOSIS	5 (10%)	7 (16%)	7 (14%)
#GASTRIC MUCOSA	(48)	(45)	(49)
HYPERPLASIA, FOCAL			1 (2%)
URINARY SYSTEM			
#KIDNEY	(50)	(49)	(50)
MINERALIZATION		2 (4%)	
GLOMERULONEPHRITIS, NOS	1 (2%)	1 (2%)	
PYELONEPHRITIS, NOS	1 (2%)		

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
INFLAMMATION, NOS	1 (2%)	1 (2%)	
ABSCESS, NOS		1 (2%)	
FIBROSIS	1 (2%)		
NEPHROPATHY	1 (2%)		
GLOMERULOSCLEROSIS, NOS	1 (2%)		
NECROSIS, NOS	1 (2%)		
NECROSIS, MEDULLARY		1 (2%)	
#KIDNEY/TUBULE	(50)	(49)	(50)
DEGENERATION, NOS	1 (2%)		
ENDOCRINE SYSTEM			
#PITUITARY	(41)	(36)	(39)
DILATATION, NOS	1 (2%)	1 (3%)	
HEMORRHAGE			1 (3%)
#ADRENAL	(46)	(48)	(48)
MINERALIZATION			1 (2%)
HYPERPLASIA, NOS	24 (52%)	10 (21%)	12 (25%)
#THYROID	(48)	(42)	(47)
FOLLICULAR CYST, NOS		1 (2%)	
#PANCREATIC ISLETS	(46)	(42)	(47)
HYPERPLASIA, NOS			1 (2%)
REPRODUCTIVE SYSTEM			
#UTERUS	(49)	(46)	(46)
HYDROMETRA	1 (2%)	3 (7%)	5 (11%)
INFLAMMATION, NOS	7 (14%)	5 (11%)	4 (9%)
#UTERUS/ENDOMETRIUM	(49)	(46)	(46)
HYPERPLASIA, NOS	2 (4%)		
HYPERPLASIA, CYSTIC	22 (45%)	23 (50%)	25 (54%)
#OVARY	(43)	(36)	(44)
MINERALIZATION	1 (2%)		
CYST, NOS		1 (3%)	
ABSCESS, NOS	8 (19%)	4 (11%)	5 (11%)
FIBROSIS	1 (2%)		
DEGENERATION, CYSTIC			1 (2%)

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

TABLE D2. FEMALE MICE: NONNEOPLASTIC LESIONS (CONTINUED)

	CONTROL	LOW DOSE	HIGH DOSE
NECROSIS, NOS	1 (2%)		
NERVOUS SYSTEM			
*CHOROID PLEXUS	(50)	(49)	(50)
MINERALIZATION			1 (2%)
INFLAMMATION, NOS		1 (2%)	
SPECIAL SENSE ORGANS			
NONE			
MUSCULOSKELETAL SYSTEM			
NONE			
BODY CAVITIES			
*PERITONEUM	(50)	(49)	(50)
INFLAMMATION, NOS		1 (2%)	4 (8%)
ABSCESS, NOS			1 (2%)
*PLEURA	(50)	(49)	(50)
INFLAMMATION, FIBRINOUS	1 (2%)		
ALL OTHER SYSTEMS			
NONE			
SPECIAL MORPHOLOGY SUMMARY			
NO LESION REPORTED	1	3	1
ANIMAL MISSING/NO NECROPSY		1	

NUMBER OF ANIMALS WITH TISSUE EXAMINED MICROSCOPICALLY
* NUMBER OF ANIMALS NECROPSIED

APPENDIX E

Analysis of Tara Gum

(Lot No. 897)

Midwest Research Institute

APPENDIX E

Analysis of Tara Gum
(Lot No. 897)

Midwest Research Institute

A. MELTING POINT

	Determined	Literature Values
m.p.:	200°-285°, decomp. (visual capillary) Endotherm 277°-319° (Dupont 900 DTA)	No literature references found

B. THIN-LAYER CHROMATOGRAPHY (of hydrolysis products after reaction with H_2SO_4, neutralization with $BaCO_3$, and filtration).

Plates: Silica Gel G F-254

Ref. Standards: D-Galactose and D-Mannose

Amount Spotted: 20 μg
60 μg

Visualization: Egon Stahl reagent 198 ($KMnO_4$ in NaOH)

System 1:

n-Butanol:Acetic Acid:Water (50:10:20)

R_f: 0.50 (major) (mannose)
0.40 (major) (galactose)
0.29 (major)

R_{st}: 1.00, 0.80, 0.58 (relative to mannose)
1.25, 1.00, 0.72 (relative to galactose)

System 2:

n-Butanol:Acetone:pH 4.0 buffer (40:40:20)

R_f: 0.74 (major) (mannose)
0.70 (major) (galactose)

R_{st}: 1.00, 0.94 (relative to mannose)
1.06, 1.00 (relative to galactose)

C. WATER ANALYSIS

(Karl Fischer) 12.4 ± 0.2 (δ)%

D. TITRATION BY PERIODATE OXIDATION

Modification of USP Assay for Mannitol (USP XVIII, 1970)

Samples were dissolved in 25 ml of concentrated sulfuric acid and 150 ml water in 250-ml volumetric flasks and left at room temperature for 16 hours. The solutions were then boiled for 35 minutes on a hot plate. The flasks were cooled and diluted to volume with water. Aliquots (5 ml) were transferred to 125-ml Erlenmeyer flasks and 50.0 ml potassium periodate/ sulfuric acid solution was added. All samples and a blank were heated on a steam bath for 5 hours.

Results: 86.2 ± 0.8 (δ)% compared with dextrose. (It is assumed that each mole of monomer requires 5 moles of periodate.)

E. SPECTRAL DATA

(1) Infrared

Instrument: Beckman IR-12

No literature spectrum found

(a) Cell: 1% potassium bromide pellet

Results: See Figure 5

(b) Cell: Thin film

Results: See Figure 6

(2) Ultraviolet/Visible

Instrument: Cary 118
No UV or visible absorbance detectable
Concentration: 0.1 mg/ml
Solvent: Water

No literature reference found

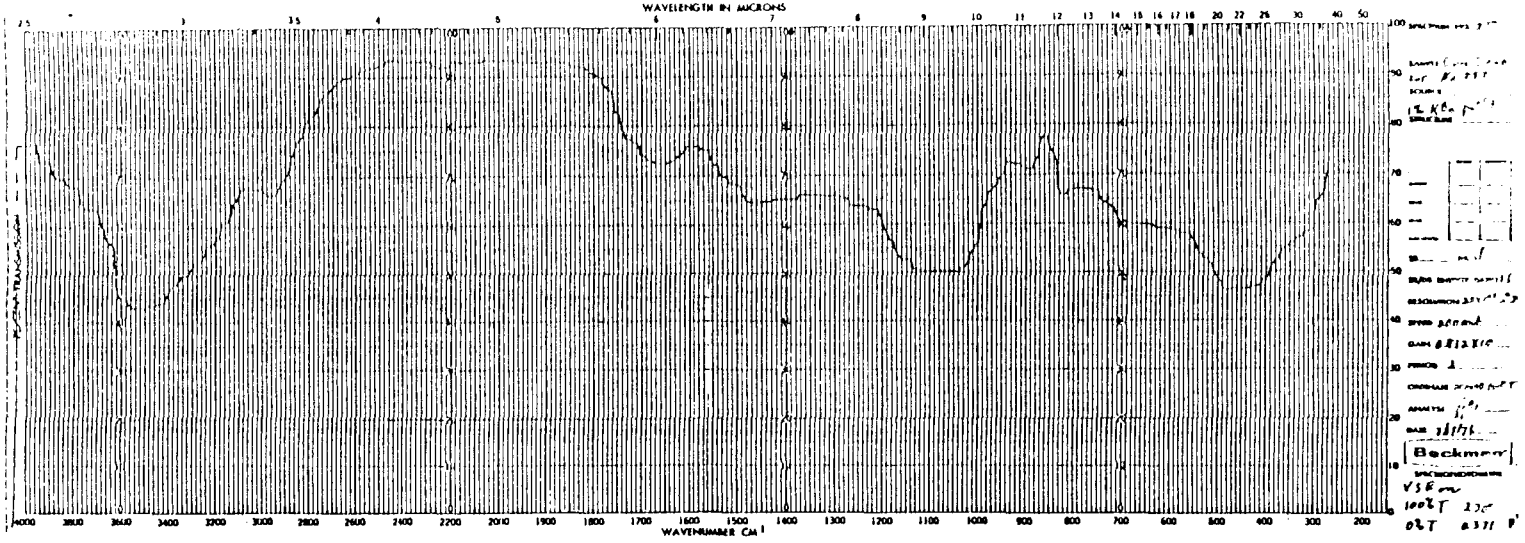

Figure 5. Infrared Absorption Spectrum of Tara Gum (Pellet)

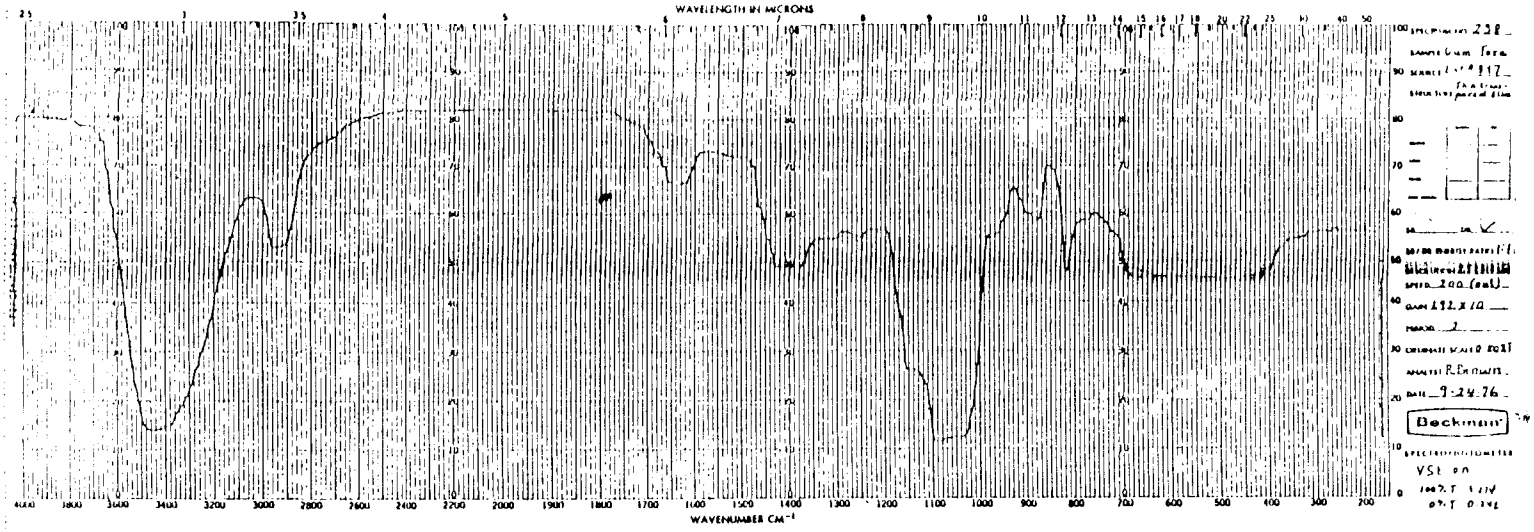

Figure 6. Infrared Absorption Spectrum of Tara Gum (Thin Film)

APPENDIX F

Feed Consumption by Rats and Mice in the Chronic Study

Table F1. Feed Consumption by Male Rats Receiving Tara Gum

WEEK	CONTROL GRAMS FEED/ DAY (a)	LOW GRAMS FEED/ DAY (a)	LOW LOW/ CONTROL (b)	HIGH GRAMS FEED/ DAY (a)	HIGH HIGH/ CONTROL (b)
4	21.7	22.3	1.0	22.9	1.1
8	18.4	18.0	1.0	19.0	1.0
12	18.3	16.9	0.9	17.6	1.0
16	18.0	18.1	1.0	21.4	1.2
20	23.1	18.9	0.8	19.4	0.8
24	22.6	19.7	0.9	20.7	0.9
28	22.1	20.1	0.9	19.0	0.9
32	23.7	21.3	0.9	20.7	0.9
36	24.0	22.6	0.9	23.3	1.0
40	24.3	21.7	0.9	21.6	0.9
44	20.6	20.6	1.0	19.4	0.9
48	24.1	21.6	0.9	21.6	0.9
52	23.9	22.4	0.9	21.9	0.9
55	24.4	19.9	0.8	21.6	0.9
60	21.7	19.1	0.9	18.6	0.9
64	28.0	26.6	1.0	26.1	0.9
68	19.7	18.3	0.9	19.4	1.0
72	19.6	17.7	0.9	17.9	0.9
76	20.4	17.7	0.9	19.9	1.0
80	22.3	18.9	0.8	19.4	0.9
83	21.6	22.9	1.1	25.0	1.2
88	21.0	19.6	0.9	20.0	1.0
92	18.9	19.1	1.0	21.0	1.1
96	21.6	20.0	0.9	20.0	0.9
100	22.1	19.6	0.9	20.7	0.9
MEAN	21.8	20.1	0.9	20.7	1.0
SD (c)	2.4	2.2	0.1	2.0	0.1
CV (d)	11.0	10.9	11.1	9.7	10.0

(a) Feed consumed per animal per day (grams).
(b) Ratio of feed per day for the dosed group to the feed per day for the controls.
(c) Standard deviation.
(d) Coefficient of variation = (Standard Deviation / Mean) x 100

Table F2. Feed Consumption by Female Rats Receiving Tara Gum

WEEK	CONTROL GRAMS FEED/ DAY (a)	LOW GRAMS FEED/ DAY (a)	LOW LOW/ CONTROL (b)	HIGH GRAMS FEED/ DAY (a)	HIGH HIGH/ CONTROL (b)
4	20.1	15.9	0.8	15.9	0.8
8	17.4	13.7	0.8	12.7	0.7
12	17.9	12.6	0.7	11.7	0.7
16	22.6	16.4	0.7	11.9	0.5
20	23.0	17.4	0.8	16.0	0.7
24	20.9	17.4	0.8	16.0	0.8
28	22.4	17.6	0.8	14.9	0.7
32	19.7	15.6	0.8	13.7	0.7
36	19.1	17.9	0.9	18.6	1.0
40	18.6	17.7	1.0	15.7	0.8
44	17.0	15.9	0.9	14.7	0.9
48	22.1	19.7	0.9	16.0	0.7
52	19.0	17.7	0.9	17.3	0.9
55	21.3	17.9	0.8	17.4	0.8
60	19.6	17.3	0.9	16.9	0.9
64	25.6	22.9	0.9	23.0	0.9
68	17.4	16.6	1.0	16.3	0.9
72	20.0	17.3	0.9	15.6	0.8
76	18.4	18.0	1.0	15.1	0.8
80	18.0	17.6	1.0	15.6	0.9
83	18.9	17.1	0.9	15.4	0.8
88	19.1	17.0	0.9	16.1	0.8
92	18.4	16.4	0.9	15.9	0.9
96	20.0	19.0	1.0	16.7	0.8
100	21.0	18.9	0.9	17.1	0.8
MEAN	19.9	17.3	0.9	15.8	0.8
SD (c)	2.1	1.9	0.1	2.2	0.1
CV (d)	10.6	11.0	11.0	13.9	12.5

(a) Feed consumed per animal per day (grams).
(b) Ratio of feed per day for the dosed group to the feed per day for the controls.
(c) Standard deviation.
(d) Coefficient of variation = (Standard Deviation / Mean) x 100

Table F3. Feed Consumption by Male Mice Receiving Tara Gum

WEEK	CONTROL GRAMS FEED/ DAY (a)	LOW GRAMS FEED/ DAY (a)	LOW LOW/ CONTROL (b)	HIGH GRAMS FEED/ DAY (a)	HIGH HIGH/ CONTROL (b)
4	6.0	6.0	1.0	6.3	1.1
8	6.1	6.7	1.1	6.6	1.1
12	6.7	6.3	0.9	6.3	0.9
16	6.0	5.9	1.0	5.9	1.0
20	7.0	5.9	0.8	6.0	0.9
24	5.7	5.7	1.0	5.9	1.0
28	5.6	5.7	1.0	6.6	1.2
32	5.6	6.1	1.1	6.4	1.1
36	7.1	7.3	1.0	7.6	1.1
40	6.6	6.7	1.0	7.3	1.1
44	7.9	8.1	1.0	8.1	1.0
48	6.7	6.9	1.0	6.7	1.0
52	7.7	3.0	0.4	7.7	1.0
56	7.3	7.4	1.0	7.4	1.0
60	6.6	7.3	1.1	6.9	1.0
64	5.9	6.1	1.0	6.6	1.1
68	5.1	5.6	1.1	5.6	1.1
72	6.6	6.1	0.9	6.3	1.0
76	7.6	7.7	1.0	7.4	1.0
80	7.6	8.0	1.1	8.1	1.1
84	8.6	8.7	1.0	8.4	1.0
88	7.6	8.1	1.1	7.6	1.0
92	9.1	8.9	1.0	8.6	0.9
96	7.6	8.1	1.1	7.6	1.0
100	6.7	7.6	1.1	8.0	1.2
MEAN	6.8	6.8	1.0	7.0	1.0
SD (c)	1.0	1.3	0.1	0.9	0.1
CV (d)	14.7	19.1	10.0	12.9	10.0

(a) Feed consumed per animal per day (grams).
(b) Ratio of feed per day for the dosed group to the feed per day for the controls.
(d) Standard deviation.
(e) Coefficient of variation = (Standard Deviation / Mean) x 100

Table F4. Feed Consumption by Female Mice Receiving Tara Gum

Week	Control GRAMS FEED/ DAY (a)	Low GRAMS FEED/ DAY (a)	Low LOW/ CONTROL (b)	High GRAMS FEED/ DAY (a)	High HIGH/ CONTROL (b)
4	7.1	7.9	1.1	7.9	1.1
8	8.1	7.6	0.9	8.1	1.0
12	9.7	8.1	0.8	8.0	0.8
16	8.7	6.9	0.8	9.4	1.1
20	7.9	7.0	0.9	8.3	1.1
24	7.7	7.0	0.9	7.6	1.0
28	7.7	7.0	0.9	11.9	1.5
32	7.4	6.7	0.9	9.3	1.3
36	9.1	9.0	1.0	9.3	1.0
40	8.7	8.1	0.9	9.0	1.0
44	10.3	8.9	0.9	9.4	0.9
48	9.0	8.0	0.9	8.6	1.0
52	10.4	8.6	0.8	9.1	0.9
56	9.9	9.1	0.9	9.7	1.0
60	7.9	9.0	1.1	7.3	0.9
64	9.1	7.6	0.8	8.1	0.9
68	5.1	5.1	1.0	5.0	1.0
72	8.1	7.4	0.9	7.9	1.0
76	9.0	8.9	1.0	8.6	1.0
80	9.3	8.4	0.9	9.0	1.0
84	11.1	9.9	0.9	9.6	0.9
88	9.4	9.0	1.0	6.7	0.7
92	9.9	9.7	1.0	9.6	1.0
96	9.3	9.1	1.0	9.6	1.0
100	8.7	8.7	1.0	9.3	1.1
MEAN	8.8	8.1	0.9	8.6	1.0
SD (c)	1.3	1.1	0.1	1.3	0.2
CV (d)	14.8	13.6	11.1	15.1	20.0

(a) Grams of feed consumed per animal per day.
(b) Ratio of feed per day for the dosed group to that for the controls.
(c) Standard deviation.
(d) (Standard Deviation/Mean) x 100.

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