EVALUATION OF THE HEALTH ASPECTS OF GUM GHATTI

AS A FOOD INGREDIENT

FEBRUARY 1973

Prepared for

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

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Life Sciences Research Office
Federation of American Societies
for Experimental Biology
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Bethesda, Maryland 20014
This report is one of a series of evaluations of the health aspects of the Generally Recognized as Safe (GRAS) food substances that are being made by the Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB) under contract with the Food and Drug Administration (FDA) of the U.S. Department of Health, Education, and Welfare. The Federation recognizes that the safety of GRAS substances is of national significance, and its resources are particularly suited to marshalling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office, established in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

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

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

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Life Sciences Research Office
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I. INTRODUCTION

Under terms of FDA Contract 72-85, FASEB's Life Sciences Research Office was requested to evaluate the health aspects of using gum ghatti as a food ingredient, primarily on the basis of information contained in a monograph furnished by FDA (1), summarizing the world's scientific literature from 1920 through 1970, and in certain supplemental documents available as of February 1973. Gum ghatti is one of the food substances that has been generally recognized as safe (GRAS) under the provisions of the Code of Federal Regulations (21 CFR 121.101, revised January 1, 1972).

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

The Select Committee on GRAS Substances of LSRO is making its evaluations of these substances in full recognition of the foregoing provisions. In reaching its conclusions on safety the Select Committee, in accord with FDA's guidelines, is relying primarily on the absence of substantive evidence of a significant risk to the public health, and realizes that a decision, based on reasoned judgment, is expected even in instances where the available information is qualitatively or quantitatively limited. The Committee is also aware that biological testing, like all of science, is dynamic. Accordingly, the Committee's decisions, based as they are on the information now available, cannot anticipate and be guided by experiments not yet done or by the results of tests that may be reconducted, using new technologies that are constantly being evolved. These decisions will need to be reviewed as new or better information becomes available.

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

Gum ghatti is obtained as an exudate from wounds in the bark of Anogeissus latifolia, a large tree found in the dry deciduous forests of India and Ceylon. The exuded "tears" are collected by hand, sun dried, and classified into grades for export. Imported gum is processed and purified, usually by grinding and sifting (1,2).

The gum, also known as Indian gum, is basically the calcium salt of ghattic acid, a complex polysaccharide containing galactose, mannose, rhamnose, arabinose, xylose, and glucuronic acid (2). The exact chemical structure is complex and has not been determined. Gum ghatti has been reported to contain a linear arrangement of 1,6-linked D-galactopyranose units (2). The water soluble portion, which accounts for over 90 percent of the gum, has been reported to have a molecular weight of 11,860 (3).

Domestic consumption of gum ghatti includes considerable nonfood use, primarily in oil-drilling muds, but it is also used in drugs and cosmetics. It is employed only to a limited extent, primarily as a stabilizer for oil-in-water emulsions in frozen dairy products and non-alcoholic beverages in proportions of 0.200 to 0.045 percent. It is also reported to be used in butter-containing table syrup (1,2,4).

A little more than 4,000 pounds of gum ghatti were reported to be used by the food industry in 1970 (4). However, the Select Committee has no information concerning the poundage used in prior years nor any information to indicate whether the gum ghatti content of the foregoing food categories has changed significantly in recent years.

III. CONSUMER EXPOSURE DATA

A comprehensive survey by a National Research Council subcommittee has provided information on the possible daily human intake of gum ghatti in the total diet, as shown in the following table for individuals in various age groups (4). The Select Committee has converted these figures to possible intake per kilogram of body weight.
<table>
<thead>
<tr>
<th>Age group</th>
<th>Possible daily intake</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Average</td>
<td>Maximum</td>
</tr>
<tr>
<td></td>
<td>mg</td>
<td>mg</td>
<td>mg</td>
</tr>
<tr>
<td>0-5 mos.</td>
<td>3</td>
<td>6</td>
<td>&lt;1</td>
</tr>
<tr>
<td>6-11 mos.</td>
<td>27</td>
<td>90</td>
<td>3</td>
</tr>
<tr>
<td>12-23 mos.</td>
<td>61</td>
<td>178</td>
<td>6</td>
</tr>
<tr>
<td>2-65+ yrs.</td>
<td>116</td>
<td>305</td>
<td>2</td>
</tr>
</tbody>
</table>

*Calculations based on an average weight of 60 kg for an adult (5) and the following estimated weights of infants by age groups: 0-5 mos., 5 kg; 6-11 mos., 8 kg; and 12-23 mos., 11 kg (6).

It is recognized that the figures calculated for the daily intake of gum ghatti per kg of body weight in the age group 2-65+ years would be low for individuals from age 2 to maturity who weigh less than 60 kg. For example, the daily intake of a child weighing 20 kg could be, on the average, 6 mg per kg rather than 2 mg, and at maximum, 15 mg per kg rather than the 5 mg indicated in the foregoing table.

However, such possible deviations from the figures in the table must also be considered in respect to total quantity of gum ghatti used in foods. The NRC subcommittee has pointed out that its calculations of intakes in most cases are overstated, often by considerable margins.* That human intakes are overstated in the case of gum ghatti is borne out by the following calculation: The NRC subcommittee has provided data that indicate the use of gum ghatti for food purposes in the United States was 4466 pounds (2030 kg) in 1970. This figure is reported to comprise between 60 and 70 percent of the total poundage used in food. On the basis of 60 percent adjusted to 100 percent (7443 pounds or 3383 kg), and a U.S. population of 200 million, the per capita per day average intake would be 46 micrograms rather than the 116 mg indicated in the foregoing table. It is separately reported that 200,000 pounds (90,909 kg) were used in foods in 1967 (2,7). Using this larger figure, the per capita per day average intake would still be only 1.24 mg.

*An explanation for such overstatements is detailed in Section XI, "Significance and Use of Data in Safety Evaluations," of the NRC subcommittee's report (4). The Select Committee finds this explanation reasonable, and concurs in the first recommendation in Section XII of the same report, that "In order to conduct a more accurate survey on the intake of substances used in food processing, food consumption data collected specifically for this purpose are needed."
On the basis of these considerations, therefore, the Select Committee regards the figures in the table as levels that are not likely to be achieved by any of the age groups.

IV. BIOLOGICAL STUDIES

Very little biological and toxicological data are available on gum ghatti in animals or man. Nothing is known about the absorption, distribution, metabolism or excretion of the gum in man or in animals and no short-term or long-term feeding experiments in laboratory animals have been reported. Tests on mutagenicity and teratogenicity of gum ghatti have only recently been completed (8,9).

Mutagenic tests on rats and mice using three different methods gave negative results. There was no measurable mutagenic response or alteration in the recombination frequency for Saccharomyces cerevisiae in either the host-mediated assay or the associated in vitro tests. No adverse effects were observed on either metaphase chromosomes from rat bone marrow or anaphase chromosomes from in vitro cultures of human embryonic lung cells at any of the doses or time periods tested. No significant adverse responses were noted in the dominant lethal gene test on rats (8).

Teratologic tests on four species of animals were negative. Oral intubation of up to 1700 mg of gum ghatti in anhydrous corn oil to pregnant mice from day 6 through day 15 of gestation exerted no clearly discernible effect on nidation or on maternal or fetal survival. The frequency of abnormalities in either the soft tissues or skeletal tissues of the fetuses in the test groups did not differ from those occurring spontaneously in the sham-treated controls. The same negative reaction was exhibited by pregnant hamsters administered up to 1700 mg per day from day 6 through day 10 of gestation. In the case of rats dosed in a similar manner (day 6 through day 15 of gestation), no untoward results were obtained at levels up to 370 mg per kg. At 1700 mg per kg, however, 5 out of 24 dams died; the surviving rats bore their living young to term and delivered healthy litters. A comparable response to that in rats was shown by pregnant rabbits at 33 mg per kg and 150 mg per kg, respectively, dosed from day 6 through day 18 of gestation (9).

It should be noted that in connection with the mutagenicity studies cited above (8), gum ghatti was administered to rats by oral intubation in anhydrous corn oil in doses of 10 g per kg for one day and 5 g per kg for five successive days. None of the 10 male Sprague-Dawley rats (weighing 200-250 g each) in either experiment died. The oral toxicity for multiple doses was reported to be greater than 5 g per kg (8).
No evidence that gum ghatti is allergenic has been reported.

V. OPINION

There is no evidence that consumption of gum ghatti by man has adverse effects when used at present levels. However, this presumption of lack of hazard is based primarily on the absence of evidence of human toxicity, rather than on substantive evidence supporting this conclusion. In view of the sparseness of toxicity data, the Select Committee attaches greater possible significance to the preliminary evidence indicating the maternal toxicity of gum ghatti at very high oral doses to pregnant rats and rabbits than it might otherwise accord these few data. It may be advisable, in due course, to conduct feeding studies in several animal species, including pregnant animals, at dosage levels that approximate and exceed the current estimated maximum daily human intake.

The Select Committee has weighed the foregoing and concludes that:

There is no evidence in available information on gum ghatti that demonstrates a hazard to the public when it is used at levels that are now current and in the manner now practiced.
VI. REFERENCES CITED


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May 31, 1973

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