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SCOGS II-23

EVALUATION OF THE HEALTH ASPECTS OF OAT GUM, OKRA GUM, QUINCE SEED GUM, AND PSYLLIUM SEED HUSK GUM AS FOOD INGREDIENTS

1982

Prepared for

Bureau of Foods
Food and Drug Administration
Department of Health and Human Services
Washington, D.C.

Contract No. FDA 223-78-2100

LIFE SCIENCES RESEARCH OFFICE
FEDERATION OF AMERICAN SOCIETIES
FOR EXPERIMENTAL BIOLOGY
9650 Rockville Pike
Bethesda, Maryland 20014

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NOTICE

This report, one of a series concerning the health aspects of using the Generally Recognized as Safe (GRAS) or prior-sanctioned food substances as food ingredients, is being made by the Federation of American Societies for Experimental Biology (FASEB) under contract no. 223-78-2100 with the Food and Drug Administration (FDA), U.S. Department of Health and Human Services. The Federation recognizes that the safety of GRAS substances is of national significance, and that its resources are particularly suited to marshaling the opinions of knowledgeable scientists to assist in these evaluations. The Life Sciences Research Office (LSRO), established by FASEB in 1962 to make scientific assessments in the biomedical sciences, is conducting these studies.

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

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

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

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I. INTRODUCTION

This report concerns the health aspects of using oat, okra, psyllium seed husk, and quince seed gums as food ingredients. It has been based partly on the information contained in a scientific literature review (monograph) furnished by FDA (Handler and Bauer, 1978), which summarizes the world's scientific literature from 1920 through 1978. To ensure completeness and currency as of the date of this report, this information has been supplemented by searches of over 30 scientific and statistical reference sources and compendia that are generally available; use of new, relevant books and reviews and the literature citations contained in them; consideration of current literature citations obtained through computer retrieval systems of the National Library of Medicine; searches for relevant data in the files of FDA; and by the combined knowledge and experience of members of the Select Committee and the LSRO staff. In addition, announcement was made in the Federal Register of April 21, 1981 (46 FR 22810) that opportunity would be provided for any interested person to appear before the Select Committee at a public hearing to make oral presentation of data, information, and views on the health aspects of using oat, okra, quince seed, and psyllium seed husk gums as food ingredients. No requests were received for presentations on oat, okra, or quince seed gums. A request was received from one company to present a statement on psyllium seed husk gum and the Select Committee held a hearing on this gum on September 14, 1981. The individual who presented a statement is identified at the end of this report. The material presented at the hearing has been considered by the Select Committee in reaching its final conclusions.

As indicated in the Food, Drug, and Cosmetic Act [21 USC 321(s)], GRAS substances are exempt from the premarketing clearance that is required for food additives. It is stated in the Act and in the Code of Federal Regulations (Office of the Federal Register, 1980b) [21 CFR 170.3 and 170.30] 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. These sections of the Code also indicate that expert judgment is to be based on the evaluation of results of credible toxicological testing or, for those substances used in food prior to January 1, 1958, on a reasoned judgment founded in experience with common food use, and is to take into account reasonably anticipated patterns of consumption, cumulative effects in the diet, and safety factors appropriate for the utilization of animal experimentation data. FDA recognizes further [21 CFR 170.30] that it is impossible to provide assurance that any substance is absolutely safe for human consumption.

The Select Committee on GRAS Substances of LSRO reviewed and evaluated the available information on oat, okra, psyllium seed husk, and quince seed gums in full recognition of the foregoing provisions. In reaching its conclusions on safety, the

Committee, in accordance with FDA's guidelines, relied primarily on the absence of substantive evidence of, or reasonable grounds to suspect, a significant risk to the public health. While the Committee realized that a conclusion based on such reasoned judgment is expected even in instances where the available information is qualitatively or quantitatively limited, it recognized that there can be instances where, in the judgment of the Committee, there are insufficient data upon which to base a conclusion. This report is intended for the use of FDA in determining the future status of these substances under the Federal Food, Drug, and Cosmetic Act. The Committee anticipates that its conclusions will be reviewed as new information becomes available.

II. BACKGROUND INFORMATION

Gums have been broadly defined by Whistler (1973) as "hydrophilic or hydrophobic high-molecular-weight molecules usually having colloidal properties, that in an appropriate solvent or swelling agent produce gels, highly viscous suspensions or solutions at low dry substance content." Substances meeting this definition and having application in food processing are hydrophilic plant or microbial polysaccharides or derivatives of such complex carbohydrates. The four gums evaluated in this report are from oat, okra, quince seed, and psyllium seed husk.

Information on oat, okra, and quince seed gums is sparse, and there are large gaps in knowledge commonly regarded as important in the evaluation of the health aspects of such products. Whistler (1973) reviewed the available data, but both chemical and biological studies are limited for each of these three gums. In contrast, considerable information on the biological properties of psyllium seed husk gum was available to the Select Committee. The Select Committee on GRAS Substances has considered the health aspects of use of gums from other vegetable sources in the following reports: carob bean gum (SCOGS, 1972a); gum tragacanth (SCOGS, 1972b); gum arabic (SCOGS, 1973a); sterculia gum (SCOGS, 1973b); carrageenan (SCOGS, 1973c); gum ghatti (SCOGS, 1973d); guar gum (SCOGS, 1973e); agar-agar (SCOGS, 1973f); and gum guaiac (SCOGS, 1975).

GRAS Status

The vegetable gums addressed in this report have been accorded GRAS status as food ingredients, by virtue of a GRAS letter or by being an optional ingredient in the identity standards of processed foods (Senti, 1980). Oat gum is listed in the 1980 Code of Federal Regulations (Office of the Federal Register, 1980a) as an optional ingredient in standards of identity for pasteurized cheese spread [21 CFR 133.175], pasteurized cheese spread with fruits, vegetables, or meats [21 CFR 133.176], pasteurized neufchatel cheese spread with other foods [21 CFR 133.178], pasteurized process cheese spread [21 CFR 133.179], and pasteurized process cheese spread with fruits, vegetables, or meats [21 CFR 133.180]. In the 1974 Code of Federal Regulations (Office of the Federal Register, 1974) oat gum and psyllium seed husk gum were listed as optional ingredients in frozen desserts [21 CFR 20]. Okra gum was given GRAS status by FDA letter (Wulfsberg, 1960), and quince seed gum received GRAS status under the category of natural extractives (solvent-free) used in conjunction with spices, seasonings, and flavorings [21 CFR 182.40] (Office of the Federal Register, 1980b).

Composition

Oat gum is a component of the flour and bran of oats (*Avena sativa*). Extraction of oat flour under alkaline conditions ~~yielded 3.5-4.2% gum, 70-87% of which was β-glucan (Wood et al.,~~ 1977, 1978). Glucose was the major monosaccharide component, with small amounts of arabinose, xylose, and possibly uronic acid (Wood et al., 1977). Earlier studies also indicated the presence of a water-soluble glucan composed of β-1,3- and β-1,4-glucopyranosyl units in aqueous extracts of oats (Acker et al., 1955; Morris, 1942; Peat et al., 1957), and small amounts of xylose and arabinose in a hydrolyzate of an unpurified aqueous extract (Preece and Mackenzie, 1952). Component sugars of water-soluble and water-insoluble, nonstarchy polysaccharides of oat flour and bran were identified by MacArthur and D'Appolonia (1980). The water-soluble portions of both flour and bran were predominantly β-glucans. Glucose (89% in flour and 93% in bran) and small amounts of arabinose (7 and 5%) and xylose (4 and 3%) were present following hydrolysis. The water-insoluble, nonstarchy polysaccharides also contained glucose as the principal monosaccharide (63% in flour and 67% in bran), but larger amounts of arabinose (23 and 19%) and xylose (14%) were detected in this fraction.

Okra gum is a complex polysaccharide obtained from okra (Hibiscus esculentus), a plant widely grown in the southern United States for food. A unique property of okra gum is the ropiness or stringiness it gives to water solutions. Large molecular aggregates present in okra gum dispersions were shown by electron photomicrographs to be branched-chain structures more than 4μ in length (BeMiller, 1973). Published reports do not fully agree as to the composition of okra gum. Whistler and Conrad (1954a,b) found two disaccharides, 4-O-D-galactopyranosyl-D-galactose and 2-O-(D-galactopyranosyluronic acid)-L-rhamnose, and two trisaccharides, D-galactopyranosyl-(D-galactopyranosyluronic acid)-L-rhamnose and (D-galactopyranosyluronic acid)-L-rhamnopyranosyl-D-galactose, in a partially hydrolyzed water extract of fresh okra. An alkaline-soluble preparation of okra gum was reported to contain D-galactose, L-arabinose, L-rhamnose, and D-galacturonic acid in a molar ratio of 80:3:10:6 (Amin, 1956). Methylation analysis revealed only methylated products of galactose and rhamnose (Amin, 1956). In contrast, Kelkar et al. (1962) found a nitrogen-containing fraction composed of amino acids and an ash portion containing calcium and phosphate that seemed to be integral parts of the gum. Other workers (Kishida, 1969; Kishida and Fukui, 1967) found that the gum contained D-glucose, D-fructose, amino acids, and a glycopeptide.

Psyllium seed husk gum is obtained from the husk of a variety of species of the genus Plantago. The plant is grown mainly in countries bordering the Mediterranean and in India. A limited amount is found in the southwestern United States. The gum content of the plant is about 12-30% (BeMiller, 1973) and compositions of polysaccharides in a number of Plantago species have been characterized. Gum from these species appears to contain varying proportions of D-xylose, D-arabinose, D-rhamnose, D-galactose, D-galacturonic acid, 4-O-methyl-D-glucuronic acid, and 2-O-(α-D-galactopyranosyluronic acid)-L-rhamnose (Anderson and Fireman, 1935; Erskine and Jones, 1956; Laidlaw and Percival, 1949, 1950; Nelson and Percival, 1942). Determinations of the exact composition of purified gums have not been made (BeMiller, 1973).

Quince seed gum is a water extract of the seed of the quince (Cydonia oblonga), a fruit widely cultivated in temperate climates throughout the world. The gum content of the seed is about 20% by weight, but labor costs have prevented production of the gum in the United States (BeMiller, 1973). Quince seed gum consists of cellulose microfibrils embedded in an amorphous polysaccharide matrix (Husemann and Kelich, 1969). Mild hydrolysis of the gum produces cellulose, L-arabinose, and two aldobiouronic acids: D-xylose combined with mono-O-methylhexuronic acid or hexuronic acid (Bailey and Norris, 1932; Renfrew and Cretcher, 1932).

Specifications for food grade products, such as those furnished in the Food Chemicals Codex (National Research Council, 1981), have not been found for any of these gums. In 1978, the Joint FAO/WHO Expert Committee on Food Additives (1978) stated that information on oat gum was insufficient to allow evaluation of the substance as a food additive.

Uses

Oat gum is not produced on a commercial scale because of low yield and difficulty in extraction (Anderson, 1980a). Although it has received GRAS status for specified uses, it appears to have no commercial use at present.

Okra gum is not commercially available (Anderson, 1980b; BeMiller, 1973) and thus has no established uses in the United States. Among potential applications cited by BeMiller (1973) were use as a whipping agent for reconstituted dried egg white, an inhibitor to sucrose crystal formation, a component in adhesives, a deflocculant in paper or fabric production, a brightening agent in electroplating, and a component of a plasma replacement preparation.

Although the primary use of psyllium seed husk gum is as a bulk-type laxative and has been used for this purpose since 1930 (BeMiller, 1973; Fingl, 1975) this report considers only its use as a food ingredient. Psyllium seed husk gum has also been used in cosmetic products such as hair-setting lotions, in paper and textile manufacture as a deflocculant, and as an emulsifying agent. Possible uses of the free acid form of the gum include treatment of gastric hypoacidity, in enteric coating materials, or in sustained-release drug preparations, removal of exogenous sodium from the gastrointestinal tract, and inhibition of bacterial growth by its pH effect (BeMiller, 1973).

Quince seed gum is used primarily by the cosmetics industry in such products as wave-setting lotions, mascara, and cleansing creams (BeMiller, 1973). It has few food applications, and its high cost would probably make such uses uneconomical. Experimentally, the gum has been used successfully as a stabilizer in chocolate milk and ice cream (Hadary and Sommer, 1943).

III. CONSUMER EXPOSURE DATA

Surveys by the National Research Council--Phase II in 1972 and Phase III in 1979--on the usage of food additives in processed foods yielded no information on okra gum, oat gum, psyllium seed husk gum, or quince seed gum (Committee on GRAS List Survey--Phase III, 1979; Subcommittee on Review of the GRAS List--Phase II, 1972).

The Select Committee has also learned that there are apparently no current food uses of psyllium seed husk gum (Meer, 1980; Peterson and Johnson, 1978) and no commercial production of oat gum (Anderson, 1980a; Meer, 1980) or okra gum (Anderson, 1980b; BeMiller, 1973). Glicksman (1969) stated that "although psyllium seed gum and quince seed gum have also been utilized to some extent in the food industry, they still find their most extensive uses in the related pharmaceutical and cosmetic industries." Young (1981) reported that approximately 4 million people of the U.S. use a commercial pharmaceutical formulation of psyllium seed husk gum and 4% of these users have taken 1-3 doses (containing about 1.8-5.3 g psyllium seed husk gum) daily for more than 20 yr. Estimated sales of this formulation in 1980 were about 33 million kg (950 million doses). In a comprehensive review of industrial gums (BeMiller, 1973), no food uses were included for psyllium seed husk, quince seed, or okra gums.

IV. BIOLOGICAL STUDIES

Absorption and metabolism

The Select Committee is not aware of any information on the absorption and metabolism of any of the vegetable gums included in this report.

Acute toxicity

Fraschini (1978) reported acute toxicity and other toxicological studies (discussed in other sections of this report) with three commercial (Metamucil®) formulations of purified psyllium seed husk gum (Plantago ovata, Forsk). The formulation designated "powder" contained 49% psyllium seed gum, 49.7% glucose, 0.6% citric acid, 0.25% monobasic potassium phosphate, 0.3% sodium bicarbonate, and 0.04% benzyl benzoate. A second, designated "instant dose," contained 56% psyllium seed gum, 16% citric acid, 14% sodium bicarbonate, 13% sucrose, 0.5% lemon flavoring, and 0.2% sodium saccharin. The third, designated "without sugar," contained 45% psyllium seed gum, 22% glycine, 21% sodium glycinate, and 12% citric acid.

The formulations, in aqueous suspension, were administered by gavage to groups of five male and five female Swiss mice (20-23 g body wt) or Sprague-Dawley rats (120-140 g) in doses of 1.5, 3.0, and 6 g/kg body wt. No deaths occurred within the 7-d observation period. Slight sedation during the first few hours was observed in animals after administration of the highest dosage. Diarrhea occurred in mice given 6 g/kg body wt of the "powder" formulation. This effect was attributed by the investigators to the high percentage of glucose in the formulation.

No information on the acute toxicity of oat, okra, and quince seed gums was available to the Select Committee.

Short-term studies

One laboratory has reported that a water-soluble fraction prepared from defatted fresh okra, with sodium chloride added to a concentration of 0.85%, can serve in hemorrhaged dogs as a partial replacement for blood plasma (Benjamin et al., 1951). The preparation had a solids concentration of 2%. The authors stated that urinary output was not affected and there appeared to be no adverse reaction to the okra preparation following infusion. None of the product was detected in tissues, but refined methods for detection were apparently not used (Benjamin et al., 1951).

In an early study, MacKay et al. (1932) reported a gray-black color in the kidneys of rats and dogs fed diets containing 25% Plantago psyllium for 125 and 30 d, respectively. The epithelial cells of the kidney tubules of the rats contained fine brown granules, but those of the dogs showed no similar changes. Thienes and Hall (1941) observed a dose-related brown pigmentation in kidneys of rats and cats fed diets containing 0, 4, or 19% crushed psyllium seed in the form of psyllium-agar flakes. Urea clearance of rats was not affected by psyllium feeding.

Coulston and Seed (1956) also carried out feeding experiments with ground psyllium seed, commonly called blond psyllium seed (P. ovata) and certain fractions of the seed. One preparation, Mucilose®, a commercial product, apparently was essentially psyllium seed gum, although the purity was not established. Sprague-Dawley rats fed for 28 wk a commercial laboratory ration to which the gum fractions were added at the 10% level were normal in growth, appearance, and behavior as compared with controls fed the basal diet alone. The rats given Mucilose® exhibited a mild laxative effect. Upon macroscopic examination, the investigators observed a dark brown color only in the kidneys of rats fed the fraction of the seed hulls from which the mucilaginous (gum) fraction had been removed. No pigment was found upon histologic examination. The authors speculated that pigmentation of the kidney might be related to a fraction of the hull. They concluded that the lack of reports of kidney pigmentation in necropsies of persons who had ingested psyllium is good evidence that humans are not affected, or that pigmentation is so minimal that it is not recognizable histologically.

Ershoff (1977) examined effects of addition of 10% (10 g/kg body wt) blond psyllium seed powder, carrot root powder, alfalfa leaf meal, or wheat bran to low-fiber purified diets containing 5% (5 g/kg body wt) tartrazine (FD&C Yellow No. 5) or Sunset Yellow FCF (FD&C Yellow No. 6). Each of these diets or the basal low-fiber purified diet was fed to groups of six male weanling Sprague-Dawley rats for 14 d. Weight gains, general appearance, and mortality rates of the groups fed the food dyes were improved when psyllium seed powder, carrot root powder, alfalfa leaf meal, or wheat bran was incorporated into the diet. Ershoff (1977) did not identify a substance in any of these materials that was responsible for the improvements in weight gain, appearance, and mortality rates, but speculated on several possible mechanisms of action.

Groups of three male and three female beagles, 10-12 mo old, were fed 250 or 750 mg/kg/d of purified psyllium seed husk gum (P. ovata) for 6 mo; results of examinations at 1, 3, and 6 mo were reported by Mercatelli et al. (1979a,b,c). The gum was described as a granular powder, light brown in color, containing dark brown particles and 3.5% impurities. The desired dose was soaked in water and then mixed with a portion of the food given to the dogs. Biochemical, urinary, and hematological tests were conducted at 0, 1, 3, and 6 mo. There were no statistically significant differences in body weight gains or food consumption between the treated and control groups at 1, 3, or 6 mo. No changes related to treatment were observed at these time intervals in hematological urinalysis of samples taken at 0, 8, and 16 wk. Blood cholesterol levels were lower in the treated groups at 16 wk. The investigator reported that histological examination revealed no changes of importance in the heart, lungs, liver, spleen, kidneys, adrenals, thyroid, pancreas, testes, ovaries, or gastrointestinal tract.

Effects of psyllium seed hydrocolloid on bile composition in rats and hamsters have also been investigated. Beher and Casazza (1971) added 0 or 4% of a bulk laxative, Metamucil®, containing about 50% psyllium seed hydrocolloid (20 g psyllium seed hydrocolloid/kg diet; about 0.9 g/kg body wt/d) to stock diets containing 5% fiber of an unspecified source. These diets were fed to groups of eight rats for 3 wk before intraperitoneal injection of [^{14}C]cholic acid or [^{14}C]chenodeoxycholic acid. Addition of psyllium seed hydrocolloid increased the turnover rate of both deoxycholic and chenodeoxycholic acids and increased the size of the chenodeoxycholic acid pool. Groups of 18 hamsters fed a gallstone-inducing diet with the addition of 5% psyllium seed hydrocolloid (2.25 g/kg/d) developed no gallstones, whereas those whose diets were not supplemented with psyllium seed hydrocolloid had seven gallstones at the end of 1 mo (Bergman and van der Linden, 1975). The concentration of deoxycholic acid and the ratios of cholic:chenodeoxycholic acid and cholic:deoxycholic acid were increased in hamsters fed the diet supplemented with psyllium seed hydrocolloid.

Long-term studies

Lifetime feeding studies in rats of several "bulk-formers" (Carlson and Hoelzel, 1948) included diets containing mixtures of psyllium seed husks (3.3% or 5%) and semi-fibrous cellulose flour or ground kapok. The authors reported that these diets "apparently introduced nothing of a deleterious nature." Rats fed these diets had longer lifespans than rats fed the basal low-residue diet, but the number of rats (2-3 of each sex fed each diet) was too small to provide conclusive data.

Human studies

Meyer and Calloway (1977) observed gastrointestinal responses of six healthy women 65-73 yr of age following administration of low-residue formula diets alone or with the addition of wheat bran, oat bran, oat gum, or raffinose. Oat gum was added in amounts (6.2 or 12.4 g) to supply 5 or 10 g/d (90 or 180 mg/kg) of indigestible carbohydrate. Elimination was somewhat more frequent and fecal weight and percentage dry solids were slightly increased over control observations after consumption of the diet containing oat gum for 3 d. Fecal water-holding capacity, as calculated by difference between wet and dry fecal weight, was less for oat gum than for oat or wheat bran. Breath hydrogen production was increased, although not significantly, following the oat gum treatment. Because the time when hydrogen production started to increase was similar to that of the control diet, the authors reported that oat gum did not appear to have a short-term fermentable component (Meyer and Calloway, 1977).

Thienes and Hall (1941) observed nine persons who had taken 7-14 g psyllium-agar flakes daily for 2-7 yr. Urea clearance tests and chemical analysis and microscopic examination of urine samples were within normal limits, and the authors reported no clinical evidence of kidney dysfunction. More recently, Spiller et al. (1979), in a double-blind experiment, studied effects of psyllium seed hydrocolloid, a cellulose-pectin mixture, or a placebo (corn syrup solids) in 50 healthy adults aged 25-65 yr who were known to have low average daily fecal weights. The psyllium seed preparation consisted of 50% psyllium seed hydrocolloid and 50% glucose. Following a 14 d baseline period 12 subjects were given 20 g of the psyllium preparation daily for 20 d (intake of psyllium seed hydrocolloid 10 g/d or approximately 140 mg/kg/d). Feces were collected on the last 7 d of the baseline and experimental periods. A low-residue diet was fed throughout the study. Fecal calcium, magnesium, and nitrogen excretions did not differ significantly for subjects given either treatment or placebo. Hematologic and blood chemistry values were within normal limits and occurrence of flatulence, gastrointestinal cramping, abdominal fullness, nausea, urgency to eliminate, headache, tiredness, weakness. Hunger was similar for all groups.

Brydon et al. (1979) administered 30 g/d (approximately 210 mg/kg/d) of a preparation containing about 50% psyllium seed hydrocolloid (Metamucil®) for 3 wk to 11 adult patients with uncomplicated gallstone disease. No changes were observed in concentration of lithocholic, chenodeoxycholic, deoxycholic, or cholic acids in bile or in acid-cholesterol ratios. In contrast, Beher et al. (1973) reported that administration of 12 g/d (approximately 200 mg/kg) of psyllium seed hydrocolloid to six post-cholecystectomy patients for 6-29 d gradually increased the concentration of deoxycholate in the bile.

Mazzola and Cappuccilli (1978) administered formulations of purified psyllium seed husk gum (P. ovata) described in the Acute toxicity section (see p.7) to 31 patients for the treatment of chronic constipation or bowel irregularity. The patients were hospitalized for bronchopulmonary and cardiac diseases, generally complicated by other pathology such as diabetes or hypertension. Diabetic patients were given a formulation not containing sugar. In severe cases of constipation, 12.8 g of "instant dose" formulation providing 7.2 g psyllium seed husk gum was given three times a day for 7-14 d. As a maintenance dose, or in less severe cases, 6.4 g of the formulation (3.6 g psyllium seed husk gum) was given three times daily. Treatment during hospitalization ranged from 11-59 d, and during outpatient treatment from 15-59 d. Average number of days to restore normal bowel action was 4.4 ± 0.37.

Mean cholesterol level of 13 patients with hypercholesteremia decreased from an initial level of 329 mg/dl to 239 mg/dl at the end of the treatment. Mean cholesterol level of the other 18 patients, 210 mg/dl, was not significantly changed by the treatment. No adverse changes attributable to treatment were observed in hematological indices (hemoglobin, red or white corpuscle count) or blood chemistry (glucose, urea, serum glutamic oxalacetic transaminase, serum glutamic pyruvic transaminase, bilirubin, alkaline phosphatase).

Davi and Strano (1978) administered 7 g, three times daily for 10 d, of psyllium seed gum formulations described in the preceding paragraph to 15 patients (average age 63.7 ± 3.2 yr) with chronic constipation. Five patients had diabetes mellitus or fasting hyperglycemia and were given the psyllium gum formulation not containing glucose. Regularity of bowel action was induced in all patients. Levels of plasma cholesterol and triglycerides were reduced at 10 d, but the decrease was statistically significant ($P < 0.05$) only for triglycerides. Levels of serum glutamate oxalacetic and serum glutamic pyruvic transaminases were significantly lower ($P < 0.05$) after treatment, but no statistically significant changes were noted in hematological parameters or in blood glucose, urea, bilirubin, or nonprotein nitrogen concentrations.

Giovannini and Careddu (1978) administered psyllium seed husk gum formulations to 10 patients with constipation (group 1), average age 13.5 mo (range, 2 mo to 4 yr) and 10 with diarrhea (group 2), average age 9.9 mo (range, 1 mo to 2 yr), for periods of 10-14 d. Composition of the formulations administered are described in the Acute toxicity section (see p.7). Five of the patients in group 1 received 3.2 g (1.8 g psyllium seed husk gum) doses of the "instant dose" formulation twice daily; the other five received two 4 g (1.8 g psyllium seed husk gum) doses of the formulation not containing sugar. All patients in group 2 received two 4 g doses of the latter formulation daily. The treatment produced a marked euperistaltic effect, bowel action being normalized in both groups. No statistically significant changes occurred in mean values of hematological or blood chemistry parameters.

Allergic symptoms (rhinitis, sneezing, conjunctival itching, and dermal itching) were reported in two nurses dispensing a bulk laxative powder containing psyllium seed husk gum and in 8 of 20 subjects challenged with psyllium seed hydrocolloid (Machado et al., 1979). Asthma and rhinitis were also noted in three workers in a pharmaceutical plant where psyllium seeds were processed (Busse and Schoenwetter, 1975).

Reproduction and teratogenicity

Studies on embryo-fetal toxicity and teratogenicity of the "powder" and "instant dose" formulations of purified psyllium seed husk gum described in the Acute toxicity section (see p.7) were reported by Fraschini (1978). The formulations, in aqueous suspension, were administered daily by gastric intubation to 10 gravid Sprague-Dawley rats and 10 gravid New Zealand white rabbits on days 6 to 15 and 6 to 18 after conception, respectively. Dosages of the "powder" formulation were 0.5 and 1.0 g/kg body wt and 0.5 g/kg body wt for the "instant dose" formulation. Necropsy of the rats on day 20 and the rabbits on day 30 of gestation revealed no significant differences between treated and control groups in the number of implantations or resorptions, or in number and weight of live fetuses. There were no dead or underdeveloped fetuses in the treated animals and no external, internal, or skeletal malformations were found in the live fetuses.

Psyllium seed (P. ovata) husk gum was administered by oral intubation to New Zealand rabbits from the 6th to 18th days of gestation (Mercatelli et al., 1978). The animals received 0, 200, or 400 mg/kg body wt/d of the gum suspended in a 1/3 v/v mixture of water and polyethylene glycol 400. The dams were sacrificed on the 30th day of gestation and fetuses and reproductive organs were examined. No differences were noted in food consumption and body weights of the gravid females. No differences were reported in numbers of live young, stillbirths, abortions, resorptions, or external, skeletal, and visceral abnormalities of the fetuses. One fetus in the high-dose group had a small tail and bifurcation of the sternebra (an indicator of variation in ossification), an abnormality occurring at the frequency of 0.5 per 1000 in the rabbit.

Carcinogenicity and mutagenicity

The Select Committee has no information on the possible carcinogenicity or mutagenicity of okra, oat, quince seed, and psyllium seed husk gums.

V. OPINION

Psyllium seed husk gum has been widely used in this country as a bulk laxative since approximately 1930. The acute toxicity of the gum is very low. Short-term animal feeding studies, including reproduction and teratogenicity studies, have demonstrated no adverse effects. Clinical studies on the effect of the gum on bowel action have revealed no significant side effects. There are no official specifications for a food-grade product and little, if any, appears to be used as an ingredient in processed foods.

The Select Committee has considered the foregoing and concludes that:

> There is no evidence in the available information on psyllium seed husk gum that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when it is used at levels that are now current or that might reasonably be expected in the future.

Three vegetable gums under consideration, oat gum, okra gum, and quince seed gum, are derived from products that have been used in human dietaries for many generations. The Select Committee has located one report concerning gastrointestinal response of women to oat gum, but has been unable to locate other reports of relevant experimental studies on the biological effects of ingesting these gums. No official specifications for food-grade products appear to exist for any of these vegetable gums and it appears that little, if any, are used as food ingredients in this country.

In light of the foregoing, the Select Committee concludes that:

> In view of the deficiency of relevant biological studies, the Select Committee has insufficient data upon which to base an evaluation of oat gum, okra gum, and quince seed gum should they be used as food ingredients.

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

PUBLIC HEARING ON PSYLLIUM SEED HUSK GUM
September 14, 1981

A presentation was made by James Young, Ph.D., Searle Research and Development Division, G.D. Searle & Company, Chicago, IL.

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