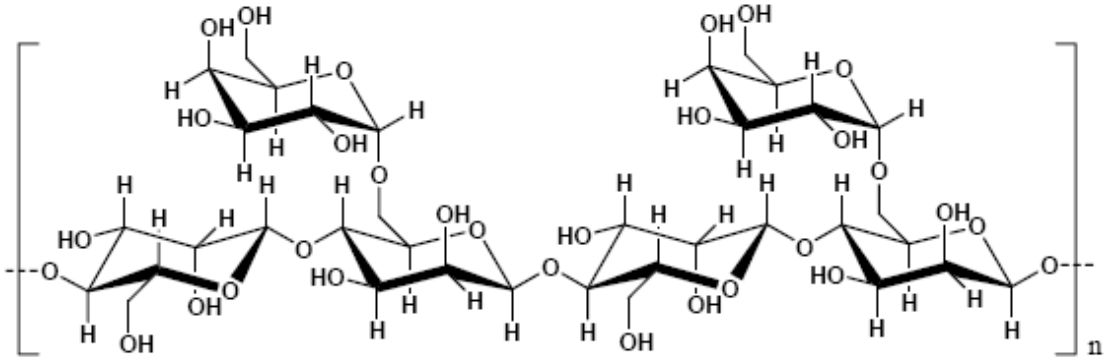
GUAR GUM (and depolymerised)

SYNONYMS

Burtonite V-7-E
Cluster Bean (*Cyamopsis spp*.)
Cyamopsis psoraloides
Cyanopsis tetragonoloba L
Guar Flour
Guar Powder
Guar gum depolymerised
Gum Cyamopsis
Gum Guar
Jaguar
Regonol

CHEMICAL STRUCTURE



CHEMICAL FORMULA

Guar gum is a galactomannan composed of a straight chain of D-mannose with a D-galactose side chain at approximately every other mannose unit. The mannose-galactose ratio is about 2:1, and the molecular weight approx. 220,000 to 250,000.

Partially depolymerised guar gum is produced from guar gum by one of three manufacturing processes which consist of heat treatment, acid hydrolysis or alkaline oxidation, which all exert a partial depolymerisation of the native guar gum. The result is guar gum which is chemically cut into smaller molecular weight sizes and has different viscosity properties (EFSA 2007).

IDENTIFIER DETAILS

CAS Number	:	9000-30-0, 68411-94-9,(78615-64-2; Dihydrogen Phosphate Guar Gum)
CoE Number	:	166
FEMA	:	-
EINECS Number	:	232-536-8
E Number	:	E412

CLP CLASSIFICATION

Ingredient CLP Classification: No

Endpoint	Classification	Category
Acute Oral Toxicity	-	-
Acute Dermal Toxicity	-	-
Acute Inhalation Toxicity	-	-
Skin Corrosive/irritant	-	-
Eye Damage/Irritation	-	-
Respiratory Sensitisation	-	-
Skin Sensitisation	-	-
Mutagenicity/Genotoxicity	-	-
Carcinogenicity	-	-
Reproductive Toxicity	-	-
Specific Target Organ Toxicity	-	-
Aspiration Toxicity	-	-

SPECIFICATIONS

Melting Point: Ill defined (complex mixture)

Boiling point: Ill defined (complex mixture)

PURPOSE

Binder

STATUS IN FOOD AND DRUG LAWS

CoE limits:

Beverages (mg/kg)	Food (mg/kg)	Exceptions (mg/kg)
-	-	-

Acceptable Daily Intake:

ADI (mg/kg)	ADI Set by	Date Set	Comments
NOT SPECIFIED	JECFA	1975	ADI not limited

FDA Status:[CFR21]

Section Number	Comments
184.1339	Guar gum

HUMAN EXPOSURE

Natural Occurrence: Guar gum is derived from the seed of the guar plant, *Cyamopsis tetragonolobus*, a leguminous plant which resembles the soybean plant. India and Pakistan are the major sources of supply, although the U.S. is also a producer. The guar is a hardy and drought-resistant plant, which grows 3 to 6 feet high with vertical stalks. The guar pods, which grow in clusters along vertical stems, are about 6 inches long and contain 6 to 9 seeds. The endosperm, which comprises 35 to 42% of the seed, is the source of the gum [Fenaroli, 1995]

Reported Uses: Guar gum is reportedly used in foods e.g. baked goods at 1.96 ppm, breakfast cereals at 11.26 ppm, cheese at 7.83 ppm and processed vegetables at 10.75 ppm [Fenaroli, 1995]. Guar gum is widely used as a food stabiliser. [NTP, 2002]

General purpose food additive, thickening agent and stabiliser: Listed in The Miscellaneous Food Additives Regulations 1995 (No. 3187) under Schedule 1 - Miscellaneous additives generally permitted for use in food.

Sources other than foods: Used as a binding and disintegrating agent in tablets, as a thickener in lotions and creams, as an appetite depressant and used in certain antihypercholesterolemic preparations [Leung *et al.,* 1996].

TOXICITY DATA

Baker *et al.,* [2004]; examined the effects of the addition of 482 tobacco ingredients upon the biological activity and chemistry of mainstream smoke. The ingredients, essentially different groups of flavourings and casings, were added in different combinations to reference cigarettes. The addition of guar gum at 100 ppm was determined not to have affected the mutagenicity of the total particulate matter (TPM) of the smoke in either the Ames, *in vitro* micronucleus assay or the neutral red assay when compared with that of the control cigarettes [Baker *et al.,* 2004].

In Vivo Toxicity Status

Guar gum is thought to have effects similar to those of cellulose, *i.e.* it protects against chemically induced carcinogenesis, modulates ricin toxicity, lowers serum cholesterol, affects mineral excretion and absorption, lowers blood pressure and affects protein absorption [Sax 1984].

Test Type	Route	Species	Reported Dosage
LD_{50}	oral	rat	6770mg/kg
LD_{50}	oral	rat	9400mg/kg
LD_{50}	oral	mouse	8100mg/kg
LD_{50}	oral	rabbit	7000 mg/kg
LD_{50}	oral	hamster	6000mg/kg

[Sax, 1984]

Sprague Dawley rats fed a diet of 5 % guar gum partially hydrolysed guar gum

and cellulose and other dietary fibres for a period of three weeks revealed guar gum to cause a significant decease in food intake, weight gain and increase in liver weight. Additionally epidydimal adipose tissue weight was significantly higher in guar gum fed rats than those fed cellulose. No significant effect was noted on serum lipids however, serum IgG was significantly lower than those animals fed cellulose. IgA and IgG productivity in mesenteric lymph node (MLN) lymphocytes were reported to be significantly higher in rats fed guar gum, glcomannan and pectin (in comparison with those fed cellulose) but Ig productivity in spleen lymphocytes was not reported to be marked. Guar gum was the only substance reported to significantly increase IgM productivity in MLN lyphocytes when compared with rats fed cellulose. These results were reported to suggest ' enhancement of the immune function by dietary fibre is mainly expressed in the gut immune system', [Yamada *et al*., 2003].

In a petition made to EFSA, data from a 90-day toxicity study for two oxidised depolymerised guar gums prepared by alkaline hydrolysis was presented. Although these studies were performed using guar gum products produced under different conditions of manufacture than those of the present opinion the petitioner indicated that the very similar structure of the depolymerised guar gum products to native guar gum suggested that toxicological evaluations of the products manufactured much earlier were still relevant for the current product. Specifications on these two preparations were provided by the petitioner and included moisture (11.8 and 13.7%), crude protein (3.6 and 2.8%), crude fibers (2.2 and 1.7%), ash (1.7 and 4.7%) lipids (0.11 and 0.09%), gum content (91.4 and 89.5%) and negative for peroxide. These partially depolymerised guar gums prepared by alkaline hydrolysis were added to the daily diet of male and female weanling rats at levels of 0 (control), 20 or 50 g/kg foodestimated to amount to doses of respectively 0, 1000 or 2500 mg/kg bw/day for a period of 90 days. Growth, food consumption, chemical, clinical and histopathological examination of theexposed animals indicated that no adverse effects were observed that were attributable to the test substance (EFSA 2007).

Carcinogenicity and mutagenicity

Guar gum has been shown to be negative in an NTP carcinogenesis assay, in both male and female, mice and rats. Feeding studies were conducted using a dose of 25,000 or 50,000 ppm Guar gum in the diet of 50 F344 rats and 50 $B6C3F_1$ mice of either sex for 103 weeks. At week 20 in mice & 40 in rats, the mean body weights of high-dose females was reduced compared with control groups. No adverse effects relating to the compound were observed. Incidence of pituitary adenomas was increased in male rats and pheochromocytomas of the adrenal gland in female rats. However, these results were not considered to be related to the administration of Guar gum. Statistical analysis of both types of tumour failed to demonstrate a link and the incidence of hepatocellular carcinomas [in mice] was significantly lower than controls. The authors conclude that Guar gum is not carcinogenic to male or female rats or mice [NTP, 1982].

In a tumour inhibition study, male Sprague-Dawley rats received an oral dose of 10% Guar gum in a fibre-free diet for 24 weeks, followed by 12mg/kg bw 1/wk 1,2-dimethylhydrazine [a known carcinogen] for 8 weeks [the study was a total of 32 weeks). The authors concluded that there were no significant differences between groups for bodyweight and that Guar gum did not significantly reduce the incidence of rat colon adenocarcinoma. [Heitman *et al.*, 1992].

Reproductive and developmental toxicity

Olejeme *et al.,* (1992) studied the effect of cellulose, wheat bran and Guar gum on the development of rat foetuses and weaned offspring. The rats were separated into nine groups of six rats. Three groups received a diet supplemented with Guar gum at 5%, 10% and 15% respectively. On day 16 of the study, a sample of each group was sacrificed and the foetuses and placentas were removed, weighed and examined. The remainder of the dams were allowed to deliver and nurse their offspring until weaned. Of those rats receiving Guar gum at 10% or more, the weight gain of the dams was significantly lower than other groups. The total number of ossification centres in the foetal skeleton of those pups from the two higher Guar gum groups was significantly lower than the other groups. However, few pups from those 2 groups survived until weaning compared with groups receiving different dietary supplements. [Olejeme *et al*., 1992].

In an FDA sponsored study, Guar gum showed no clear evidence of teratogenic potential on gross examination of chicken embryos. However, a LD_{50} of 0.05 mg Guar gum dissolved in water per egg was established when it was injected into the yolk sac at 0 hours [Verrett *et al.*, 1980]. The authors do not discuss the significance of these findings.

In an earlier teratogenesis study, the authors concluded that Guar gum was not a teratogen. Male and female Osborne-Mendal rats received Guar gum in the diet at 0, 1, 2, 4, 7.5 or 15 % ad lib. for 13 weeks before mating, during mating and throughout gestation. During gestation, 0, 0.7, 1.4, 2.7, 5.2 or 11.8g Guar gum/kg bw/day, respectively, was consumed by the females. All animals were sacrificed on gestation day 20. No behavioural effects were seen during the experiment, except for a decrease in appetite compared with controls but this was not dose related. Pre-pregnancy dosing of Guar gum did not effect fertility. There was no effect on the number of corpora luteal or implantation's in Dams receiving Guar gum up to a level of 7.5%. However, in the high dose group [15%], the number of corpora lutea and implantation's were slightly reduced although there was no effect on implantation efficacy. The number of viable foetuses/litter was also not significantly reduced, and since the number of resorptions was not affected, the decrease would appear to be an effect of the reduced number of corpora lutea. The authors also state that there was no compound-related effect on foetal development or sex distribution [Collins *et al*, 1987].

Inhalation toxicity

A standard textbook also states that occupational asthma has been reported in people working in the industrial production of Guar gum [Leung *et al.,* 1996].

Bush *et al.,* (1990) cite a paper by Malo, which describes Guar gum as having a high molecular weight and therefore being associated with occupational rhinitis and asthma, with 5-8% of carpet factory workers sensitive to Guar gum. Bush *et al.* therefore question the importance of Guar gum as an occupational hazard in the food industry [Bush *et al*., 1990].

The addition of guar gum at 100 ppm to reference cigarettes, used in a 90 day-sub-chronic inhalation exposure in rats, led to a series of pathological changes to smoke exposure that were indistinguishable from those changes caused by the control cigarettes. This indicated that addition of guar gum to a reference cigarette had no discernable effect upon the type or severity of the treatment related pathological changes associated with tobacco smoke exposure [Baker *et al.,* 2004]

When tested at in cigarettes, in a 13-week inhalation study, the presence of guar gum had no discernible effect on the character of extent of the biologic responses normally associated with inhalation of mainstream cigarette smoke in rats."[Gaworski *et al.*, 1998] [however, it should be noted that the cigarettes had been spiked with a number of flavour ingredients in combination prior to smoking, and they contained a typical American blend humectant and sugar component (*i.e.* glycerine ≈ 20,000 ppm, propylene glycol at ≈ 24,000 ppm, and brown invert sugar at ≈ 24,000 ppm)] [Gaworski *et al.*, 1998].

Other relevant studies

In summary significant safety data on guar gum have been published. These include a 103-week carcinogenicity study in rats and mice up to 50 g/kg in the diet, which was preceded by a subchronic study at doses up to 100 g/kg diet, and a developmental toxicity study in rats up to150 g/kg diet (NTP 1982a; Melnick *et al.* 1983). Guar gum when given to F344/N rats or B6C3F1 mice at dietary levels of 25 or 50 g/kg (amounting to about 1250 or2500 mg/kg bw/day for rats and 3600 and 7200 mg/kg bw/day for mice) for 103 weeks did not induce cancer (NTP, 1982a; Melnick *et al.,* 1983). The No Observed Adverse Effect levels for each of these studies was the highest dose tested (EFSA 2007).

Nicolosi *et al* (2001) discussed several dietary cardiovascular disease risk factors, in particular the association of increased cholesterol and an increased risk of coronary heart disease, and the importance of dietary intervention. They site a paper by Jones *et al* (1994) that demonstrates the significant cholesterol-lowering effect of dietary Guar gum in rats [Nicolosi *et al*, 2001].

Tobacman *et al*., (2000) Investigated the consumption of carrageenan and other water-soluble polymers commonly used as food additives, and their association with the incidence of mammary carcinoma. The authors concluded that there was no significant positive correlation between the

increased consumption of Guar gum and mammary carcinoma. [Tobacman *et al* 2000].

Guar gum taken as a supplement [as opposed to smaller amounts used as a food additive] is thought to increase the viscosity of the bowel content, resulting in the feeling of postprandial fullness, and therefore may reduce appetite. Clinical trials suggest that Guar gum may lower body weight and the medical literature suggests oral treatment for overweight patients. Guar gum containing preparations are freely available as slimming aids, both in the USA and Europe. However, a meta-analysis of randomised trials suggests a non-significant difference between patients receiving Guar gum and those receiving a placebo. Eleven trials were statistically pooled out of the 34 trials identified by the authors, and they point out that 3% of patients dropped out of the trials because of the adverse effects produced by Guar gum supplements. These include abdominal pain, flatulence, diarrhoea and cramps. No information is given regarding the dose level or frequency of the Guar gum supplements taken [Pittler & Ernst, 2001].

The ministry of Health, Labour and Welfare recommend Japanese people to intake a certain amount of dietary fiber, believing that incorporating more dietary fiber into the diet can reduce the risk of colorectal cancer. During two fourteen-day sessions in spring and autumn, 9 healthy female students took the same diets. During the first session, the students were provided a strict dietary formula, while during the second session, they were administered an 12.5 g/day of partially hydrolysed guar gum (PHGG, purity 80%, equivalent to 10 g of dietary fibre) dissolved in adequate amount of water at the end of each meal. There were no adverse reactions to the treatment reported. PHGG intake resulted in increase of the fecal bulk for 4 subjects and fecal moisture for 5 out of 9 subjects, but decreased fecal hardness in 3 subjects; the benefit of bowel movements provided by the PHGG intake, however, varied greatly among the subjects [Sakata *et al.,* 2006] .

High-fibre diets have been associated with effecting the caloric intake and bioavailability of essential minerals and trace elements. Guar gum is often used as a thickener in infant formula milk. Using a dialysis machine calibrated to reflect the digestive capabilities of infants, Guar gum has been shown to decrease the availability of calcium, iron and zinc [Bosscher *et al*. 2001].

A brief metabolic study demonstrates the above affect on iron absorption in rats. The absorption of radiolabelled iron by jejunal segments of both normal and iron deficient rats was inhibited by an oral dose of Guar gum. The highest dose administered, 30 mg, inhibited absorption by 25% [Woelbling *et al*, 1980].

Grizard *et al* (2001) studied insulin and corticosterone level changes produced by Guar gum. Three groups of 9 male Wistar rats were fed different experimental diets for 3 weeks. These diets consisted of AIN-76 formulations in which 10 % [w/w] wheat starch was replaced with either sucrose, Guar gum or LMM-pectin at the same concentration. For those rats receiving the Guar gum diet, a significant growth rate reduction was noted [by 24%] compared

with controls. This is likely to have been brought about by the effects of dietary Guar gum on lipid absorption. Blood triacylglycerine was strongly reduced [by 76% compared with controls] and total cholesterol was reduced by 39%. In addition, postprandial insulin concentrations were significantly reduced without altering postprandial glucose levels and glucagonemia was up-regulated. The authors discuss the mechanisms of action of Guar gum to produce these effects demonstrating that they are all linked to the bulk & high viscosity of Guar gum modifying the diffusion of nutrients. They also site Morgan *et al* (1979) who shows that humans fed Guar gum also have a resulting decrease in insulin secretion and production of gastric inhibitory polypeptide [Grizard *et al.,* 2001].

A similar study to that of Grizard *et al., (2001*) demonstrated that a diet including Guar gum decreases the absorption of trichloroethylene [TCE] in rats. In this instance by 12 % compared with groups fed similar meals. The rats were fed a meal of Guar gum – docosahexaenoic acid for 3 weeks and then given a single oral dose of 100 mg TCE. Analysis was then carried out 10 hours later [Nakashima *et al*. 2001].

Another study investigating the dietary effects of Guar gum in human volunteers demonstrates that no significant effect on either systemic appearance of dietary amino acids, or plasma and urinary dietary urea kinetics, occurred following the consumption of ^{15}N-labelled protein meal [30 g soy protein] containing 1% high-viscosity Guar gum. However, there was an early effect on endogenous urea kinetics [Mariotti *et al.*, 2001].

Following the inclusion of up to 59.6 g/day Guar gum into the diet of 6 insulin dependent diabetic volunteers, a small reduction in cholesterol levels occurred. Guar gum was taken daily for 4-6 weeks and the results compared against the previous 2 weeks as a control [Carroll *et al.*, 1981].

A standard text book states that in women, ingestion of Guar gum resulted in permanent weight loss without effecting serum lipids in hypercholesterolemia, and that similar observations occurred in both male & elderly patients. However, in diabetics, positive results are reported in use of Guar gum as a long-term dietary supplement, in control of hypercholesterolemia. The text also reports that long-term administration [21g/day] of Guar gum produced a sustained improvement of Type 2 diabetes, significantly lowering serum total and LDL cholesterol concentrations. On average, total cholesterol was reduced by 14 % immediately before meals as well as by 16% in postprandial glucose levels. The text also refers to a human study on patients with diabetes mellitus, where Guar gum consumption did not adversely affect mineral balance. However, flatulence has been commonly reported as a Guar gum side effect [Leung *et al.,* 1996].

A study to develop a colon-specific delivery system for mesalazine (5-ASA) using a guar gum carrier using X-ray imaging revealed that the matrix tablets reached the colon and was not subjected to disintegration in the upper region of the GI system in all of the 8-subjects involved, [Tugcu-Demiroz *et al*., 2004].

A study in which the effects of partially hydrolysed guar gum, (PHGG) in yogurt, (containing 6g PHGG) on the elevation of postprandial serum lipid levels, (11-male subjects) suggested that their was 'potential for PHGG to reduce the risk of hyperlipemia', [Kondo *et al*., 2004].

An in vivo pharmacolkinetic study (in humans) revealed that a guar gum-based colon-targeted formulation did not release the drug in the stomach and small intestine, but delivered it to the colon which resulted in the slow absorption of the drug therefore making it available for local action in the colon, [Krishnaiah *et al*., 2003].

All depolymerised guar gum preparations have average molecular weights that match the criteria set for the molecular weight of food grade guar gum specified to be between 50 000 g/mol and 8 000 000 g/mol by the EU and FAO/WHO/JECFA. The galactose to mannose (G/M) ratio of all preparations is typically between 0.5 and 0.66 and there was no difference in G/M ratio between the native and the depolymerised gums. The chromatograms of the sugars after complete hydrolysis of the guar gum indicated that the sugar profile is identical in native and depolymerised guar gum .(EFSA 2007).

In the petition made to EFSA, it states that the partially depolymerised guar gum products are very similar to native guar gum with respect to structure and composition, and that the chemical processes used to obtain the reduction in molecular weight are sufficiently mild as not to introduce residual contaminants and/or to result in a significant difference in the quality and quantity of residual contaminants that are found in native guar gum Given the processing conditions of the depolymerised guar gum, certain amounts of salts are formed as a result of the neutralization step in the process. The use of sodium hydroxide to neutralise citric acid used for the acid hydrolysis step results in formation of sodium citrate. The use of phosphoric acid to neutralise sodium hydroxide used for the oxidative alkaline hydrolysis step results in the formation of sodium phosphate. These salts are permitted for use as food additives in various foods. (EFSA 2007).

Partially hydrolyzed guar gum (PHGG) is produced from guar gum and has the same chemical structure but less than one-tenth the original molecular length making it good as a film former, foam stabilizer and swelling agent. Its properties make it a beneficial dietary fibre without altering the rheology, taste, texture and colour of guar gum. PHGG is known as Benefiber(R) in the USA and has GRAS status (EFSA 2007).

A total of 95 ingredients were tested individually through addition at different concentrations to the tobacco of experimental cigarettes. Mainstream cigarette smoke chemistry analysis, bacterial mutagenicity testing, and cytotoxicity testing were conducted. The authors concluded that these ingredients, which included guar gum produced minimal changes in the overall toxicity profile of mainstream cigarette smoke, and in some cases, the addition of high levels of an ingredient caused a small reduction in toxicity

findings, probably due to displacement of burning tobacco [Gaworski *et al*., 2011].

Behavioural data:

No data identified

***In Vitro* Toxicity Status**

Carcinogenicity and mutagenicity

Guar gum has been shown to be negative in the Ames *Salmonella typhimurium* assay with and without S9 activation systems [both rat and hamster liver fractions used]. The strains tested were TA97, TA98, TA100, TA1535 and TA1537 [Zeiger *et al.,* 1988].

A paper investigating the inhibitory activity of heat treated vegetables on mutagenicity using *Salmonella typhimurium* (TA98 & TA100), suggests that the presence of water soluble indigestible polysaccharides when heated greatly increased the inhibitory action against specific mutagens. [Yamaguchi, 1992]

Guar gum failed to induce gene mutations in *Drosophila melanogaster* in a sex-linked recessive lethal mutagenesis test [Lee, 1983]

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