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Food-Grade Carrageenan: Reviewing Potential Harmful Effects on Human Health

Executive Summary

Carrageenan is derived from red seaweed, and is used as an ingredient in foods such as dairy, dairy alternatives (such as soy-based beverages and desserts) and deli meats as a thickening agent, stabilizer and/or emulsifier.

Carrageenan can be classified as low molecular weight, “degraded” carrageenan, or high molecular weight, or “undegraded” carrageenan.

Degraded, low molecular weight carrageenan is recognized as a carcinogen in lab animals, and is therefore classified as a “possible human carcinogen” by the International Agency for Research on Cancer.¹

Degraded carrageenan also causes inflammation in the colon in rodents, which resembles ulcerative colitis, an inflammatory bowel disease.² This inflammatory property of degraded carrageenan is not in dispute, especially since the medical research community has used degraded carrageenan for decades to induce acute inflammation in experimental trials conducted with lab animals, to test anti-inflammation drugs.^{3 4 5 6 7}

Carrageenan processors tend to portray the difference between degraded and undegraded carrageenan as a simple, black-and-white distinction. They claim that food-grade carrageenan sold to food processors falls entirely in the undegraded category.

However, studies (including industry-funded studies) show that food-grade carrageenan is also linked to colon inflammation and colon cancer in animals. Studies have reported that high molecular weight carrageenan can degrade in the gastrointestinal tract to low molecular weight carrageenan.^{8, 9}

Moreover, when the industry tested its food-grade carrageenan for the presence of degraded carrageenan, results showed that every sample had at least some degraded carrageenan, with some test results of food-grade carrageenan showing as much as 25% degraded carrageenan.

Timeline

1960's -present: Starting in 1961, animal studies consistently show that degraded carrageenan is carcinogenic.^{10 11 12 13 14}

1969: Researchers find that degraded carrageenan causes ulcerations and inflammation in lab animals that closely resemble ulcerative colitis, a human inflammatory bowel disease.¹⁵

1969 - present: Researchers testing treatments for ulcerative colitis use degraded carrageenan to induce the disease in laboratory animals.^{16 17 18 19}

1973: A study shows that degraded carrageenan induces inflammation in the digestive system of monkeys. This shows that degraded carrageenan affects the gastrointestinal system of primates as well as rodents.²⁰

1975: A study with rhesus monkeys finds adverse effects in the intestinal tract when the animals were given low levels (1% solution) of **undegraded** carrageenan in their drinking water.²¹

1978: A study published in *Cancer Research* finds that rats fed a diet containing **undegraded** carrageenan had higher rates of cancer than rats fed a control diet without carrageenan. The authors conclude: "**The undegraded carrageenan in the diet had an enhancing effect in colorectal carcinogenesis in rats.**"²²

1980-1981: Leading carrageenan researchers R. Marcus and James Watt publish two letters in the *Lancet*, titled "Danger of Carrageenan in Foods" and "Potential Hazards of Carrageenan," pointing out health concerns with the consumption of carrageenan, **including undegraded carrageenan.**

They note that the harmful effects of undegraded carrageenan in animals "are almost certainly associated with its degradation during passage through the gastrointestinal tract."²³

1983: With adequate scientific data showing the carcinogenicity of degraded carrageenan in lab animals, the International Agency for Research on Cancer (IARC) classifies **degraded** carrageenan as Group 2B, "*Possibly carcinogenic to humans.*"²⁴ The Agency determines that there is **not enough evidence to classify undegraded carrageenan** as a possible human carcinogen.

1986: A study finds that exposure of rats to 6% **undegraded** carrageenan in the diet for 24 weeks, with weekly injections of the carcinogenic substance 1,2-dimethylhydrazine (1,2-DMH), was associated with an **increase in tumors** from 40% to 75% and with the more frequent occurrence of larger and proximal tumors.²⁵

1995: Three scientists perform the Technical Advisory Panel (TAP) review²⁶ for the National Organic Standards Board, to determine whether carrageenan is an ingredient appropriate for use in organic foods. None of the three reviewers mentions the carcinogenicity in animal studies of degraded carrageenan, or the “possibly carcinogenic to humans” classification by the IARC. None mention the studies suggesting possible adverse health effects of undegraded carrageenan.

One reviewer downplays the potential human health effects of carrageenan by writing: “Carrageenan has a high molecular weight and must be distinguished from lower molecular weight “degraded” carrageenan which may have adverse health effects.”

The reviewers doing the 1995 TAP review do not include more recent studies (widely available in 1995) pointing to potential human health problems, such as the 1992 study by Wilcox et al, with Proctor and Gamble, that finds an association between epithelial cell loss and the consumption of both undegraded and degraded carrageenan.²⁷

1996: The National Research Council of the National Academy of Science adopts the IARC classification for degraded carrageenan (possible human carcinogen).²⁸

2001: A study finds higher levels of tumors in rats given food-grade carrageenan, yet reports that the difference is not statistically significant. This study, partially funded by the food industry, publishes its findings with the conclusive and misleading title and conclusion that food-grade, “undegraded” carrageenan is safe (despite its findings of higher cancer rates). Marinalg, the industry trade group for carrageenan processors, uses the study to reassure its customers that carrageenan is safe.²⁹

June 2001: A Joint FAO/WHO Expert Committee on Food Additives (JECFA) recommends an Acceptable Daily Intake of “not specified” for carrageenan. Marinalg hails the decision and claims it confirms the safety of carrageenan.³⁰

September 2001: Joanne Tobacman, MD, then Assistant Professor of Clinical Medicine at the University of Iowa (now Associate Professor of Clinical Medicine at the University of Illinois at Chicago), publishes an article in the academic, peer-reviewed journal *Environmental Health Perspectives*. Dr. Tobacman conducted an independent review of the scientific literature on carrageenan, and concluded: “Because of the acknowledged carcinogenic properties of degraded carrageenan in animal models **and the cancer-promoting effects of undegraded carrageenan in experimental models**, the widespread use of carrageenan in the Western diet should be reconsidered” (emphasis added).³¹

March 2003: The European Commission’s Scientific Committee on Food reviews Tobacman’s 2001 article, and reviews recent safety data on carrageenan. The Committee suggests that the amount of degraded carrageenan in food-grade

carrageenan be kept to levels below 5%, “in order to ensure that the presence of any degraded carrageenan is kept to a minimum.”³³

The Commission also reaffirms its earlier position that it remains inadvisable to use carrageenan as an ingredient in infant formula.

2005: Marinalg, the industry trade group, convenes a working group to determine the levels of degraded carrageenan in its products.³⁴ The working group tests 12 samples of food-grade carrageenan from a variety of suppliers in six different laboratories, to measure the presence of degraded carrageenan and determine if the 5% limit is feasible.

The results from the industry’s own test results are cause for serious concern. First, the levels of degraded carrageenan detected in the samples varied considerably depending on the laboratory performing the tests. This suggests that even the industry does not have a reliable way of determining the levels of degraded carrageenan in food-grade carrageenan.³⁵ If the carrageenan manufacturers have no reliable way of testing levels of degraded carrageenan in their products, how can they claim their food-grade carrageenan is safe?

Second, the results showed that 8 of the 12 samples of food-grade carrageenan contained higher than 5% degraded carrageenan according to at least one of the laboratories (in many cases, according to multiple laboratories).

Most alarmingly, all samples contained at least some degraded carrageenan according to the majority of laboratories.

Not a single sample could confidently claim to be entirely free of the material that is classified as a “possible human carcinogen.”

The highest level of degraded carrageenan found in a sample was 25%.

2002-2012: Industry-sponsored scientists question whether the inflammatory nature of carrageenan is rodent-specific, and whether the results of animal studies can be extrapolated to humans.^{36 37} Scientists conduct experiments using human colonic epithelial cells and find that carrageenan, even low levels of food-grade carrageenan, induce inflammation in human colon cells as well.^{38 39 40 41}

2008: The National Organic Standards Board considers whether to re-allow carrageenan during the Sunset process. No public interest groups or scientists chime in. The NOSB receives ten comments from industry, including carrageenan manufacturers, the Organic Trade Association, and various organic food manufacturers using carrageenan, all claiming carrageenan is safe and essential in organic processing.⁴²

January 2012: Marinalg reports that, after eight years of planning, experimentation, and analysis (2003 to 2011), the industry has been unable to reliably measure the levels of degraded carrageenan in its products in the laboratories of its members, its customers, or in independent laboratories.⁴³

May 2012: The National Organic Standards Board again reviews carrageenan during the Sunset process, and will decide whether to continue allowing carrageenan in certified organic foods.

Q&A: Essentiality in Organic Handling

Q: Are there alternatives to carrageenan for food processors?

A: Yes. On supermarket shelves, equivalent organic products appear side-by-side with some containing carrageenan and others without carrageenan. Food processors can use organic gums, including organic guar gum and organic locust bean gum as alternatives to carrageenan.

Q: Do other gums used as stabilizers and thickening agents raise the same health concerns?

A: No. Carrageenan, unlike other gums, is highly sulfated and contains certain bonds (alpha-1,3-disaccharide bonds) which are foreign to human cells and stimulate an innate immune response. This immune response leads to inflammation, which can be chronic. In the intestine, chronic inflammation is associated with the development of malignant cancer.

Q: Is carrageenan essential in organic handling?

A: No. For every organic product on store shelves containing carrageenan, an equivalent product by another manufacturer can be found that does not contain carrageenan.

Soy Creamer: Wildwood Pulmuone “soy creamer” contains carrageenan, whereas Organic Valley “soy creamer” does not.

Soy Milk: Silk, Earth Balance and Organic Valley soymilk contains carrageenan, whereas Westsoy and Eden Foods unsweetened soymilk does not.

Low Fat Cottage Cheese: Horizon lowfat cottage cheese contains carrageenan whereas Organic Valley low fat cottage cheese uses organic guar gum and organic locust bean gum instead.

And more.... The marketplace has already shown that acceptable alternatives to carrageenan exist.

Summary

The Organic Foods Production Act of 1990 (OFPA) sought to establish an alternative food system for consumers wishing to avoid potentially dangerous substances in the food supply.

OFPA allows up to 5% (by weight) non-organic ingredients in a processed organic food, but only if “the use of such substances **would not be harmful to human health** or the environment” (OFPA Sec. 2118(c)(1)(A)(i)).

The USDA’s organic standards require the following of non-organic, non-agricultural substances allowed in organic foods: “The substance itself, **or its breakdown products**, do not have adverse effects on human health as defined by applicable Federal regulations” (emphasis added) (7 CFR 205.600(b)(3)).

The organic standards include the requirement that the substance’s “breakdown products” do not have adverse effects on human health, and industry data show that food-grade carrageenan contains levels of carcinogenic degraded carrageenan, sometimes as high as 25%. **Moreover, research shows that food-grade carrageenan can be broken down to degraded carrageenan in the gastrointestinal tract.**

Scientific evidence shows that the consumption of food-grade carrageenan may lead to harmful effects on human health, including inflammation, lesions, and cancer in the colon.

¹ <http://monographs.iarc.fr/ENG/Monographs/vol31/volume31.pdf>

² Delahunty T, Recher L, Hollander D.. Intestinal permeability changes in rodents: a possible mechanism for degraded carrageenan-induced colitis. *Food Chem Toxicol* 25:113–118. 1987.

³ IARCIARC Working Group on the Evaluation of the Carcinogenic Risk of Chemicals to Humans. Carrageenan. *IARC Monogr Eval Carcinog Risk Hum* 31:79–94. 1983.

⁴ Nicklin S, Miller K.. Effect of orally administered food-grade carrageenans on antibody-mediated and cell-mediated immunity in the inbred rat. *Food Chem Toxicol* 22:615–621. 1984.

⁵ Thomson AW, Fowler EF. Carrageenan: a review of its effect on the immune system. *Agents Actions* 1:265–273. 1981.

⁶ Salyers AA, West SHE, Vercelotti JR, Wilkins TD. Fermentation of mucins and plant polysaccharids by anerobic bacteria from the human colon. *Appl Environ Microbiol* 334:529–533. 1977.

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- ⁷ Di Rosa M.. Review: Biological properties of carrageenan. *J Pharm Pharmacol* 24:89–102. 1972
- ⁸ Pittman KA, Golberg L, Coulston F. Carrageenan: the effect of molecular weight and polymer type on its uptake, excretion and degradation in animals. *Food Cosmet Toxicol* 14:85–93. 1976.
- ⁹ Engster M, Abraham R.. Cecal response to different molecular weights and types of carrageenan in the guinea pig. *Toxicol Appl Pharmacol* 38:265–282. 1976.
- ¹⁰ Cater DB. The carcinogenic action of carrageenin in rats. *Br J Cancer* 15:607–614. 1961
- ¹¹ Ashi KW, Inagaki T, Fujimoto Y, Fukuda Y. Induction of degraded carrageenan of colorectal tumors in rats. *Cancer Lett* 4(3): 171-6. 1978.
- ¹² Mankes R, Abraham R. Lysosomal dysfunction in colonic submucosal macrophages of rhesus monkeys caused by degraded iota carrageenan. *Proc Soc Exp Biol Med.* 1975 Oct;150(1):166–170.
- ¹³ Rustia M, Shubik P, Patil K.. Lifespan carcinogenicity tests with native carrageenan in rats and hamsters. *Cancer Lett* 11:1–10. 1980.
- ¹⁴ Hopkins J.. Carcinogenicity of carrageenan. *Food Cosmet Toxicol* 19:779–788. 1981.
- ¹⁵ Watt J, Marcus R.. Ulcerative colitis in the guinea-pig caused by seaweed extract. *J Pharm Pharmacol* 21:187S–188S. 1969
- ¹⁶ Kitsukawa Y, Saito H, Suzuki Y, Kasanuki J, Tamura Y, Yoshida S.. Effect of ingestion of eicosapentaenoic acid ethyl ester on carrageenan-induced colitis in guinea pigs. *Gastroenterology* 102:1859–1866. 1992
- ¹⁷ Jensen BH, Andersen JO, Poulsen SS, Olsen PS, Rasmussen SN, Hansen SH, Hvidberg DF. The prophylactic effect of 5-aminosalicylic acid and salazosulphapyridine on degraded-carrageenan-induced colitis in guinea pigs. *Scand J Gastroenterol* 19:299–303. 1984
- ¹⁸ Watt J, Marcus SN, Marcus AJ. The comparative prophylactic effects of sulfasalazine, prednisolone, and azathioprine in experimental ulceration. *J Pharm Pharmacol* 32:873–874. 1980.
- ¹⁹ Kitano A, Matsumoto T, Oshitani N, Nakagawa M, Yasuda K, Watanabe Y, Tomobuchi M, Obayashi M, Tabata A, Fukushima R, et al. Distribution and anti-inflammatory effect of mesalazine on carrageenan-induced colitis in the rabbit. *Clin Exp Pharmacol Physiol* 23:305–309. 1996.
- ²⁰ Benitz K-F, Golberg L, Coulston F. Intestinal effects of carrageenans in the rhesus monkey (*Macaca mulatta*). *Food Cosmet Toxicol* 11:565–575 (1973)
- ²¹ Mankes R, Abraham R. Lysosomal dysfunction in colonic submucosal macrophages of rhesus monkeys caused by degraded iota carrageenan. *Proc Soc Exp Biol Med.* 1975 Oct;150(1):166–170.
- ²² Watanabe K, Reddy BS, Wong CQ, Weisburger JH. Effect of dietary undegraded carrageenan on colon carcinogenesis in F344 rats treated with azoxymethane or methylnitrosourea. *Cancer Res* 38:4427–4430. 1978.
- ²³ Marcus R, Watt J.. Danger of carrageenan in foods and *Lancet* 1:338. 1981, Marcus R, Watt J.. Potential hazards of carrageenan *Lancet* 1:602–603. 1980

²⁴ <http://monographs.iarc.fr/ENG/Monographs/vol31/volume31.pdf>

For undegraded (native) carrageenan, the IARC noted the following: "In female rats treated with azoxymethane or Nnitrosomethylurea together with **native** carrageenan in the diet, a **greater incidence of colorectal cancers** was observed than with treatment by azoxymethane or N-nitrosomethylurea alone." Yet despite this finding, the IARC classified undegraded carrageenan as "Group 3," "*Not classifiable as to its carcinogenicity to humans.*" Note that this is different from the classification of "Group 4," which is "*Probably not carcinogenic to humans*"

²⁵ Arakawa S, Okumua M, Yamada S, Ito M, Tejima S. Enhancing effect of carrageenan on the induction of rat colonic tumors by 1,2-dimethylhydrazine and its relation to β -glucuronidase activities in feces and other tissues. *J Nutr Sci Vitaminol (Tokyo)* 32:481–485. 1986.

²⁶ TAP Review on Carrageenan by Dr. Richard Theuer. Available online at <http://www.ams.usda.gov/AMSV1.0/getfile?dDocName=STELPRDC5067875&acct=nopgeninfo>. Last accessed April 4, 2012.

²⁷ Wilcox DK, Higgins J, Bertram TA. Colonic epithelial cell proliferation in a rat model of nongenotoxin-induced colonic neoplasia. *Lab Invest* 67:405–411. 1992.

²⁸ National Research Council. *Carcinogens and Anti-carcinogens in the Human Diet*. Washington, DC:National Academy Press, 1996;398

²⁹ Hagiwara A, Miyashita K, Nakanishi T, Sano M, Tamano S, Asai I, Nakamura M, Imaida K, Ito N and Shirai T. Lack of Tumor Promoting Effects of Carrageenan on 1,2-Dimethylhydrazine-induced Colorectal Carcinogenesis in Male F344 Rats. *J Toxicol Pathol Vol.* 14; 37. (2001)

³⁰ http://www.marinalg.org/PDF/1_Safety_of_carrageenan_and_processed_eucheuma_seaweed.pdf

³¹ Tobacman JK. Review of Harmful Gastrointestinal Effects of Carrageenan in Animal Experiments. *Environ Health Perspect* 109(10). 2001

³³ http://ec.europa.eu/food/fs/sc/scf/out164_en.pdf

³⁴ Status report on the work of Marinalg International to measure the molecular weight distribution of carrageenan and PES in order to meet the EU specification: less than 5% below 50,000 Daltons. Marinalg. Available online at: http://www.marinalg.org/PDF/FULL_Molecular_weight_distribution_of_carrageenan_and_PES.pdf. Last accessed April 4, 2012

³⁵ In an earlier version of the Working Group's report, Marinalg admitted: "At the time of writing (November, 2005) the Working Group has not found a method for molecular weight distribution measurement that is sufficiently accurate and reproducible to yield a validated and defensible method."

³⁶ Cohen SM and Ito M. A Critical Review of the Toxicological Effects of Carrageenan and Processed Eucheuma Seaweed on the Gastrointestinal Tract. *Crit. Rev. Toxicol.* 32(5): 413-444. 2002.

The paper is sponsored in part by Marinalg, the industry trade group for carrageenan processors.

³⁷ Carthew P. Safety of Carrageenan in Foods. *Environ Health Perspect* 110:a176-a176. 2002.

Carthew, at the time of writing this correspondence, is an employee of Unilever.

³⁸ Bhattacharyya S, Borthakur A, Dudeja PK, Tobacman JK. Carrageenan induces interleukin-8 production through distinct Bcl10 pathway in normal human colonic epithelial cells. *Am J Physiol Gastrointest Liver Physiol* 2007;292(3):G829-38. Epub 2006 Nov 9.

³⁹ Bhattacharyya S, Dudeja PK, Tobacman JK. Tumor necrosis factor alpha-induced inflammation is increased but apoptosis is inhibited by common food additive carrageenan. *J Biol Chem*. 2010 Dec 10;285(50):39511-22. Epub 2010 Oct 11

⁴⁰ Bhattacharyya S, Gill R, Chen M-L, Zhang F, Linhardt RJ, Dudeja PK, Tobacman JK. Toll-like receptor 4 mediates induction of Bcl10-NFκB-IL-8 inflammatory pathway by carrageenan in human intestinal epithelial cells. *J Biol Chem*.2008;283(16):10550-8. E pub 2008 Feb 5

⁴¹ Bhattacharyya S, Borthakur A, Tyagi S, Gill R, Chen ML, Dudeja PK, Tobacman JK. B-cell CLL/lymphoma 10 (BCL10) is required for NF-kappaB production by both canonical and noncanonical pathways and for NF-kappaB-inducing kinase (NIK) phosphorylation. *J Biol Chem*. 2010 Jan 1;285(1):522-30. Epub 2009 Nov 6

⁴² Although The Cornucopia Institute was in its fourth year of operation in 2008, our primary focus was farm policy. As we have grown and matured, and it has become obvious that there is a need for independent scrutiny of materials petitions and sunset reviews, we are committing greater resources to providing balance and oversight of the organic materials review process at the USDA.

⁴³ "Status report on the work of Marinalg International to measure the molecular weight distribution of carrageenan and PES in order to meet the EU specification: less than 5% below 50,000 daltons." Available at www.marinalg.org, last accessed April 3, 2012.