United States Department of Agriculture
Agricultural Marketing Service | National Organic Program
Document Cover Sheet
https://www.ams.usda.gov/rules-regulations/organic/petitioned-substances

Document Type:

☐ **National List Petition or Petition Update**

A petition is a request to amend the USDA National Organic Program's National List of Allowed and Prohibited Substances (National List).

Any person may submit a petition to have a substance evaluated by the National Organic Standards Board (7 CFR 205.607(a)).

Guidelines for submitting a petition are available in the NOP Handbook as NOP 3011, National List Petition Guidelines.

Petitions are posted for the public on the NOP website for Petitioned Substances.

☒ **Technical Report**

A technical report is developed in response to a petition to amend the National List. Reports are also developed to assist in the review of substances that are already on the National List.

Technical reports are completed by third-party contractors and are available to the public on the NOP website for Petitioned Substances.

Contractor names and dates completed are available in the report.

Carrageenan
Handling/Processing

Identification

Chemical Names:
carrageenan; carrageenin; iota-carrageenan; kappa-carrageenan; lambda-carrageenan

Other Names:
Carragheen gum; *Chondrus crispus*; Chondrus extract; *Eucheuma* spp.; Eucheuman (from *Eucheuma* spp.); Furcellaran or Danish agar (from *Furcellaria* spp.); *Furcellariaceae*; *Gigartinaceae*; Irish moss (*Chondrus spp.*); Irish moss extract; *Kappaphycus alvarezii;* Philippine natural grade (PNG); processed *Eucheuma* seaweed (PES); refined carrageenan (RC); semi-refined carrageenan (SRC)

Trade Names:
Aubygel™; Ceamgel®; Genu® Plus 100; Genugel®; Genulacta®; Genutine®; Genuvista®; Satiagel™; Satiagum™; Seabrid™

CAS Numbers:
9000-07-1 (general)
9062-07-1 (iota)
11114-20-8 (kappa)
9064-57-7 (lambda)
9000-21-9 (furcellaran)

Other Codes:
E Numbers: E407 (carrageenan); E407a (processed *Eucheuma* seaweed)
EC (EINECS) Numbers: 232-524-2 (carrageenan); 232-949-3 (iota); 234-350-2 (kappa); 232-953-5 (lambda)

Summary

This limited scope technical report provides updated information to the National Organic Standards Board (NOSB) to support the sunset review of carrageenan, listed at 7 CFR 205.605(a)(9). This report focuses on the manufacturing processes of carrageenan, and its reported effects on human health. Carrageenan is used in organic processing and handling as a food additive.

Carrageenan was added to the National List of Allowed and Prohibited Substances (hereafter referred to as the "National List") with the publication of the National Organic Program (NOP) final rule, *Amendments to the National List of Allowed and Prohibited Substances* (65 FR 61987, October 31, 2003). Carrageenan was originally included on the proposed rule *National Organic Program* in 1997 (62 FR 65850, December 16, 1997), but inadvertently omitted in the *National Organic Program* final rule in 2000 (65 FR 80548, December 21, 2000). The NOSB recommended the relisting of carrageenan on the National List in 2005, 2007, 2010, and 2021 (NOSB, 2005, 2007, 2010, 2021b).

In 2016, the NOSB recommended removing carrageenan from § 205.605(a) due to the availability of alternatives (NOSB, 2016b). The NOP evaluated the recommendation and determined there was a lack of available natural substitutes, and that potential substitutes did not adequately replicate the functions of carrageenan across the broad scope of its uses (83 FR 14347, April 04, 2018). As part of the 2023 (reviewed in 2021) National List Sunset Review process, the NOSB voted against removing carrageenan from § 205.605(a) (NOSB, 2021b).

As carrageenan is listed at § 205.605(a), only nonsynthetic forms are allowed. Currently, many (if not most) certifiers consider carrageenan produced from alkali extracts as nonsynthetic. Historically, the NOSB determined carrageenan to be nonsynthetic as well (NOSB, 2009). The 1995 TAP report includes brief details for both the aqueous and alkali-extraction manufacturing methods (NOSB, 1995). However, in 2012, the NOSB noted that: *"there are differing points of view as to whether or not the extraction process actually changes the physical nature of the material to the point where it should be considered a synthetic or not"* (NOSB, 2012b). The Handling Subcommittee recommended that this listing be revisited once the NOP finalized the Draft Guidance submitted by the NOSB on November 5, 2009 (NOSB, 2012b). In 2016, the Handling Subcommittee reaffirmed they would not revisit the classification question until the guidance document was final (NOSB, 2016b). In 2021, the NOSB noted that public commenters expressed interest in the NOSB revisiting the classification of this material (NOSB, 2021a).

This report provides technical information to support the NOSB's discussions about manufacturing processes and classification [see *Evaluation Question #1(C)* for details].

Characterization

Composition of the Substance:

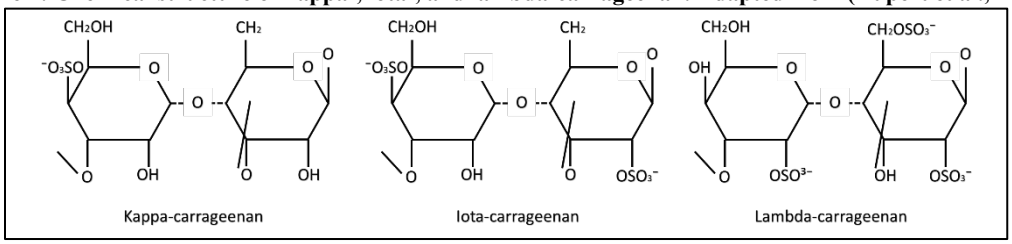
Carrageenan molecules consist of the potassium, sodium, magnesium, and calcium sulfate esters of galactose and 3,6-anhydrogalactose polysaccharide (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).

The "backbone" of carrageenan is made up of galactose molecules (monomers), bonded together to form a chain (polymer). These monomers are (Sarkar et al., 2024):

- α-1,3-linked D-galactose ("monomer A")
- β-1,4-linked D-galactose ("monomer B")
- 3,6-anhydro-α-D-galactose ("monomer C")

In carrageenan, monomer B will link with either monomer A or monomer C in a repetitive pattern to form the backbone structure (Chevenier et al., 2023). These different monomers are linked with β(1,4) and α(1,3) bridges in an alternating pattern to form the polymer chain (Sarkar et al., 2024). These monomers can exist in different forms (isomers), where hydrogens, hydroxyl groups, methyl, and carboxyl groups are oriented in different directions along the length of the molecule (see *Figure 1*).

Figure 1: Chemical structure of kappa-, iota-, and lambda-carrageenan. Adapted from (Rupert et al., 2022).



In carrageenan, sulfate is also bonded to the galactose molecules in different places via ester bonds. As sulfate groups are negatively charged, they attract positively charged ions (Campo et al., 2009). The most common positively charged ion in carrageenans include potassium, sodium, magnesium, and calcium (Campo et al., 2009).

The carrageenan isomers are commonly identified by a Greek letter and these carrageenan isomers differ depending on the number and position of sulfate groups and the presence or absence of the 3,6-anhydro-bridge on monomer A (Chevenier et al., 2023) (see *Table 1*). This bridge creates an additional molecular ring structure within the monomer. It is the presence of the 3,6-anhydro-bridge that impacts the degree of gel formation between carrageenan types (Chevenier et al., 2023).

Table 1: Carrageenan types and key chemical characteristics. Adapted from (Sarkar et al., 2024).

Carrageenan type	Backbone structure[1]	Number of sulfate groups	Position of sulfate groups
Beta (β)	Monomers B and monomers A	0	Not applicable
Gamma (γ)	Monomers A and monomers B (6S)	1	6th position of monomers A
Theta (θ)	Monomers B (2S) and monomers C (2S)	2	2nd position of monomers B and 2nd position of monomers C
Iota (ι)	Monomers B (4S) and monomers C (2S)	2	4th position of monomers B and 2nd position of monomers C
Kappa (κ)	Monomers B (4S) and monomers C	1	4th position of monomers B
Lamda (λ)	Monomers B (2S) and monomers A (2S;6S)	3	2nd position of monomers B, 2nd and 6th position of monomers A
Mu (μ)	Monomers B (4S) and monomers A (6S)	2	4th position of monomers B and 6th position of monomers A
Nu (ν)	Monomers B (4S) and monomers C (2S)(6s)	3	4th position of monomer A; 2nd and 6th position of monomers C

Manufacturers intentionally produce these three carrageenan types (kappa-, iota-, and lambda-) by selective extraction methods (see *Carrageenan's chemical changes during alkali extraction* for details). There are also other types of carrageenan, but these are not commercially significant (see *Source or Origin of the Substance*) (Das & Bal, 2024). The variations in chemical composition of the monomers and sulfate groups influence the physical

[1] Monomer A is α-1,3-linked D-galactose; monomer B is β-1,4-linked D-galactose; monomer C is 3,6-anhydro-α-D-galactose.

characteristics of carrageenan. Food producers utilize these differences for specific food applications (Imeson, 2009). For example, food producers use (Das & Bal, 2024; Rudke et al., 2020):

- kappa-carrageenan for its ability to form brittle gels.
- iota-carrageenan for its ability to form elastic gels.
- lambda-carrageenan as a thickening agent.

Kappa- and iota-carrageenan are the most common carrageenan types used by food processors (Rudke et al., 2020). Kappa-carrageenan previously accounted for approximately 67% of the global carrageenan market share by volume. Of that global market share, 78% of that carrageenan was used in the food and beverage industry (Zhang et al., 2023). We found no details related to the global carrageenan market share directly related to the organic food and beverage industry.

Source or Origin of the Substance:

Scientists have identified several isomers or types of carrageenan (Sarkar et al., 2024). All carrageenan types occur in unprocessed red algal cells (Chevenier et al., 2023). Beta-, kappa-, iota-, and lambda-carrageenan are the only types found in the algal cell wall (Chevenier et al., 2023). However, the biochemical synthesis pathway of carrageenan in red algae is still unclear, and remains an area of continuing research (Rupert et al., 2022; Sarkar et al., 2024).

Scientists currently understand that UDP-D-galactose, a carrageenan precursor molecule, forms in the cytoplasm of the algal cell and migrates from there into the Golgi apparatus.[2] Once in the Golgi apparatus, UDP-D-galactose undergoes a series of enzymatic modifications to ultimately become gamma-carrageenan (Chevenier et al., 2023; Sarkar et al., 2024). At present, it is unclear if there is an additional intermediate molecule between the conversion of UDP-D-galactose and the formation of gamma-carrageenan. Gamma-carrageenan then undergoes another series of enzymatic modifications to produce all of the other types of carrageenan (Chevenier et al., 2023; Sarkar et al., 2024). It remains unclear if formation of the 3,6-anhydro-bridge, which is present in some carrageenan types, occurs in the Golgi apparatus, cell wall, or both. At present, scientists have only biochemically characterized enzymatic activity in carrageenan related red algae from extracts of *Chondrus crispus* and *Solieria chordalis* (Chevenier et al., 2023).

Unprocessed red algae material typically contains a combination of these carrageenan types (Jouanneau et al., 2010). Furthermore, different red algae species possess different combinations of the hybrid carrageenan structures, and this can also vary with life stage (Jouanneau et al., 2010). The hybrid structures arise from the co-occurrence of several carrageenan isomers. The proportion and physical distributions of these carrageenan isomers within the algal cell reflect the carrageenan biosynthetic pathway previously described (Jouanneau et al., 2010).

- *Eucheuma* and *Kappaphycus* species contribute to over 90% of all carrageenan production (Rupert et al., 2022).
- Most kappa-carrageenan is extracted from *Kappaphycus alvarezii* (previously *Eucheuma cottonii*), which has a naturally occurring high ratio of kappa-carrageenan (Rupert et al., 2022). Consequently, this species is the most commercially important source of carrageenan (Rupert et al., 2022).
- Iota-carrageenan is mostly extracted from *Eucheuma denticulum* (previously *Eucheuma spinosum*) (Abdul Khalil et al., 2018).
- Carrageenan from *Chondrus crispus* and *Gigartina* species contains both kappa and lambda types (Imeson, 2009). Processors extract lambda-carrageenan primarily from these species (Udo et al., 2023).

Alkaline treatment of unprocessed red algae promotes the transformation of the algal cell wall material that contains only about 10% (w/v) hybrid polysaccharides to polysaccharides having almost ideal structure and at concentrations ranging from 0.1% to 1% (w/v) (see *Carrageenan's chemical changes during alkali extraction* for details) (Genicot-Joncour et al., 2009).

Furcellaria species contain both kappa- and lambda-carrageenan (Imeson, 2009). Producers purify furcellaran from these species. Furcellaran is another sulfated polysaccharide classified for food use with functional similarities to carrageenan. For this reason, furcellaran shares the same food additive number as carrageenan in European Union legislation (Imeson, 2009). However, furcellaran forms very firm, brittle gels, similar to agar, and contains 16-20% sulfate (Imeson 2009). Contrastingly, carrageenan typically contains a sulfate content of 20% or more. While carrageenan and furcellaran are related materials, the specifics of furcellaran production and its health impacts are not included in the scope of this technical report.

[2] The Golgi apparatus (or complex) is an organelle found in most eukaryotic cells that is responsible for chemically modifying proteins and packaging them into vesicles for transport throughout the cell.

Evaluation Questions

Classification of the Substance:

Evaluation Question #1(A): Describe if this substance is extracted from naturally occurring plant, animal, or mineral sources.

Carrageenan is a sulfated polysaccharide extracted from the cell wall of red algae (Rhodophyta) (Rupert et al., 2022). Carrageenan is extracted from a naturally occurring organism; however, technically speaking, that organism is not a plant or animal. Historically, the NOP has applied the term "aquatic plants" broadly to marine macroalgae, seaweed, and marine vegetation (NOP, 2025). Current taxonomic systems denote that red algae are photosynthetic eukaryotes with both unicellular and multicellular species that belong to the Archaeplastida clade (Chevenier et al., 2023). [3] Archaeplastida includes unicellular and multicellular green algae and vascular land plants. These, however, represent separate and distinct subgroups within the clade (Goodson et al., 2021).

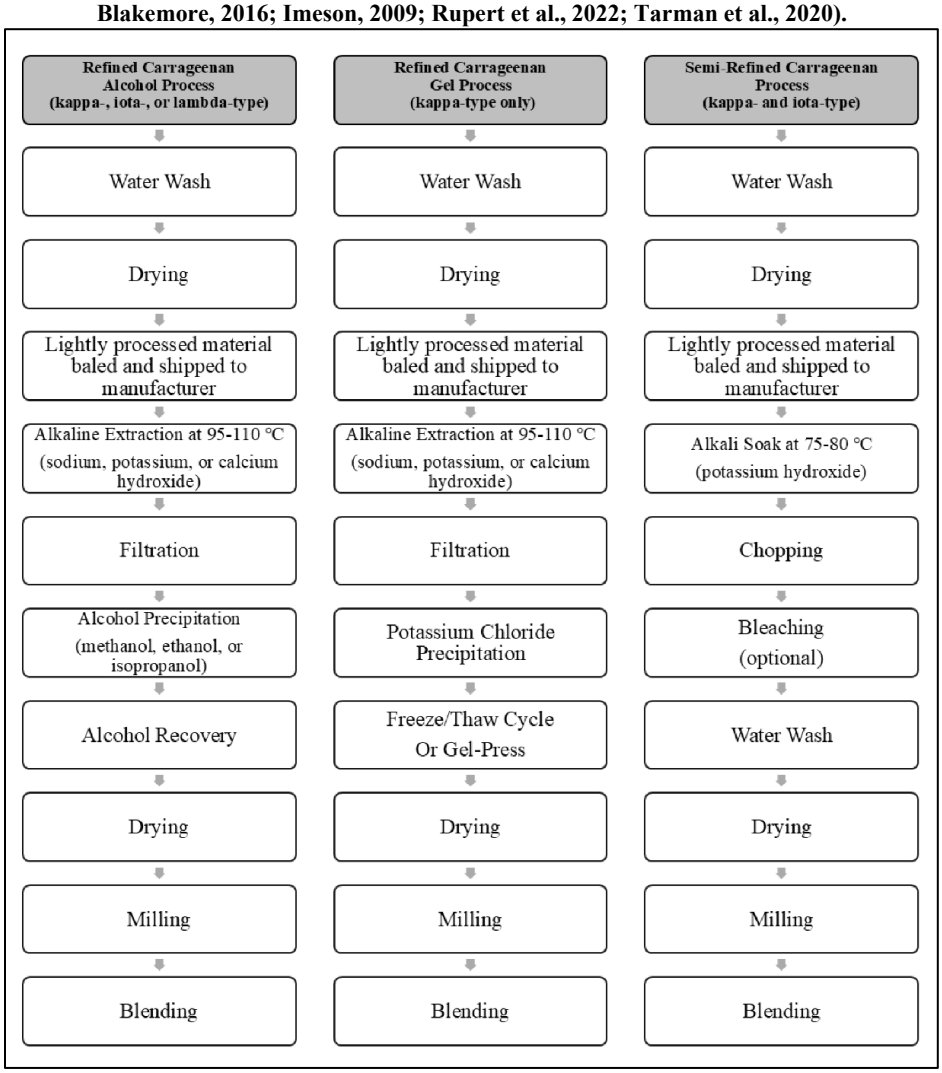
Evaluation Question #1(B): Describe the most prevalent processes used to manufacture or formulate this substance. Include any chemical changes that may occur during manufacture or formulation of this substance.

While the specific details of carrageenan extraction processes are often proprietary, most extraction processes follow one of three general methods and two grades(Das & Bal, 2024):

- alcohol process (refined grade)
- gel process (refined grade)
- semi-refined carrageenan process

The typical steps for these three methods are outlined below (see *Figure 2*).

Figure 2: Common methods to produce carrageenan from unprocessed red algae (Alba & Kontogiorgos, 2019; Blakemore, 2016; Imeson, 2009; Rupert et al., 2022; Tarman et al., 2020).



[3] Organisms whose cells have a membrane-bound nucleus.

The production process of all carrageenan begins with the selection and harvest of the raw macroalgae material from the marine environment. Processors wash the collected algae with fresh water to remove sand and salt debris, then quickly dry the washed macroalgae to prevent microbial degradation and preserve the quality of carrageenan for transport to the manufacturing plant (Rupert et al., 2022). The target range for moisture content of the dried red algae material is 18-35%, depending on the species and natural salt content from the seawater (Blakemore, 2016). The lightly processed red algae material is then typically baled and shipped to the processing plant (Rupert et al., 2022).

As of 2023, semi-refined carrageenan accounts for the majority of the global market (52%) (Zhang et al., 2023). It is also known as processed Eucheuma seaweed (PES) or Philippine natural grade (PNG) carrageenan. The manufacturing costs associated with the semi-refined process are lower compared to the refined carrageenan extraction processes (alcohol or gel processes), and produce a lower purity product (Zhang et al., 2023). In the European Union, refined and semi-refined carrageenan have distinct E-numbers and must be labelled separately (Imeson, 2009). However, in the United States and other markets, no distinction is made between these grades. We found no details describing the relative market split between refined and semi-refined carrageenan in the organic food and beverage industry.

Semi-refined carrageenan

Semi-refined carrageenan is the product of a singular common production method (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). Manufacturers produce semi-refined carrageenan by dissolving and removing the soluble compounds of the lightly processed red algae (Blakemore, 2016). The carrageenan remains a component of the seaweed algal structure, and cellulosic solids (8–15%) remain in the final product.

1. Semi-refined carrageenan processing begins with manufacturers treating the lightly processed red algae with aqueous potassium hydroxide at 75–80 °C for two hours to dissolve and remove soluble compounds other than carrageenans (Mendes et al., 2024). The presence of excess potassium cations prevents carrageenan solubility. In some cases, manufacturers may use sodium hydroxide/potassium chloride combinations (Blakemore & Harpell, 2010).
2. Manufacturers then drain the potassium hydroxide solution and rinse the carrageenan multiple times. It is common practice to reuse or recycle the alkali solution (Blakemore & Harpell, 2010). This washing step is designed to remove the potassium hydroxide and any other water-soluble compounds (*e.g.,* carbohydrates and protein) (Imeson, 2009).
3. At this point, manufacturers may add an optional bleaching step to reduce the color of the final product (Imeson, 2009). Without bleaching, the semi-refined carrageenan generally remains cloudy due to the insoluble cellulosic particulates. This can limit the feasible applications for semi-refined carrageenan (Mendes et al., 2024). Both calcium hypochlorite and hydrogen peroxide are solutions that manufacturers use to bleach the red algae material, according to information EFSA panelists received from manufacturers (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).
4. After the optional bleaching step, manufacturers wash the carrageenan with water, then dry, mill, and blend the carrageenan to produce the commercial product (Blakemore, 2016).

Refined carrageenan

Manufacturers produce refined carrageenan using either the alcohol precipitation or gel concentration methods (see *Figure 2*) (Blakemore, 2016). Alcohol precipitation produces the highest purity and most refined product (Abdul Khalil et al., 2018). Refined carrageenan can also be produced using the gel method, but at a lower cost since it does not use alcohol in the process.

As of 2023, approximately 19% of the global carrageenan supply was refined carrageenan produced by alcohol precipitation (Zhang et al., 2023). At the same time, approximately 29% of the global carrageenan supply was refined carrageenan produced using the gel method (Zhang et al., 2023).

1. Refined carrageenan production begins when manufacturers heat the lightly processed red algae material in an alkali solution for several hours at 90-110 °C (Mendes et al., 2024). This extraction method increases gel strength in the final product (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). Gelation of kappa-carrageenan and iota-carrageenan requires the presence of specific salts: potassium ions for kappa-carrageenan and calcium ions for iota-carrageenan (Blakemore, 2016). Consequently, manufacturers commonly use potassium hydroxide to extract kappa-carrageenan and calcium hydroxide to extract iota-carrageenan (Tarman et al., 2020).
2. Once the alkali extraction is complete, the pH of the alkaline liquor is adjusted (Tarman et al., 2020).
3. After the alkali extraction step, manufacturers remove any undissolved bulk algae material by centrifugation or coarse filtration (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).

4. Manufacturers then use a pressure filter on the remaining solution. The solution generated at this stage contains 1–2% carrageenan, and it is usually concentrated to 2–3% by vacuum distillation and ultrafiltration.
5. At this stage in the process, the material undergoes precipitation by either the alcohol or gel method.

Alcohol process

(continued from step 5 of *Refined carrageenan*)

6. In the alcohol precipitation method, alcohol is added until all the carrageenan is precipitated.
7. Manufacturers separate the carrageenan precipitate by centrifugation or by filtration through a fine sieve (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018), then press the carrageenan to remove the alcohol.
8. Manufacturers then dry the carrageenan and mill it to an appropriate particle size, typically 80 mesh or finer.[4]

Gel process

Manufacturers only use the gel method to produce kappa-carrageenan (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). There are a couple of key characteristics that influence this. First, this method relies on the ability of iota-carrageenan to form a gel with potassium salts, potassium chloride is typically used (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). Unlike iota- and lambda-carrageenan, kappa-carrageenan does not have freeze/thaw stability (Das & Bal, 2024). Kappa-carrageenan hydrogels also can spontaneously release fluid under certain elastic conditions. This process is called syneresis or dewatering (Ako, 2015).

(continued from step 5 of *Refined carrageenan*)

6. Processors begin the gel process by extruding the concentrated carrageenan into a potassium chloride solution (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). This produces thin, flexible rods of material with a noodle appearance.
7. Next, they collect the fine, noodle-like material and wash it with more potassium chloride.
8. Manufacturers then press the material to remove excess liquid (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018), and may continue to squeeze out water from the gel by simply applying pressure to it in the gel-press option. Alternatively, in the freeze/thaw method, the carrageenan is frozen at this stage rather than pressed. When the material thaws, the separation of the water fraction occurs by contraction of the gel fraction.
9. Manufacturers then wash the gel material once again with potassium chloride. The final product inevitably contains some potassium chloride (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).
10. The manufacturers chop the washed sheets of gel material, then dry and mill the carrageenan to an appropriate particle size.

Finished products are made by blending one or more carrageenan extracts, with or without standardizing agents [see *Evaluation Question #1(E)*], in order to maintain a consistent product.

Alternative methods of production

Manufacturers currently use large quantities of chemical solvents in the common alkaline extraction methods outlined above. There are alternative extraction methods that could possibly avoid or reduce the usage of solvents. These methods include (Rudke et al., 2020; Rupert et al., 2022):

- Microwave-assisted extraction
- Enzyme-assisted extraction
- Ultrasound-assisted extraction
- Subcritical water extraction

Researchers have demonstrated that these methods can produce carrageenan products similar to commercial grade products in the lab (Rudke et al., 2020; Rupert et al., 2022). However, we found no evidence that manufacturers use these methods for commercial production of carrageenan at the present time.

Carrageenan's chemical changes during alkali extraction

Red algae do not naturally produce the ideal, food-grade forms of kappa-, iota-, or lambda-carrageenan. Although all types of carrageenan may be found within the diversity of unprocessed red algae cells these forms exist in hybrid structures (see *Source or Origin of the Substance*) (Mendes et al., 2024). The alkali extraction step in the manufacturing process results in a concentration of ideal, food-grade carrageenan, but also results in chemical

[4] 80 mesh describes a screen filter with 80 openings across one linear inch of the surface.

changes that stabilize food-grade carrageenan. *Both the manufacturing process for semi-refined and refined carrageenan involve these chemical changes* (Rupert et al., 2022). The alkali extraction occurs in the alkali soak step for the production of semi-refined and the alkali extraction step for the production of refined carrageenan (see *Figure 2*). The chemical stabilization process enhances the following characteristics of carrageenan (Mendes et al., 2024):

- gel strength
- the material's reactivity with proteins

The gelling properties of food-grade carrageenans are influenced by the accompanying cations and the conformation of monomer units within the polymer chain (Blakemore, 2016). Gelation of kappa-carrageenan and iota-carrageenan requires the presence of specific salts: potassium ions for kappa-carrageenan and calcium ions for iota-carrageenan (Blakemore, 2016). Scientists observed in experiments that without these cations, these types of food-grade carrageenan do not form gels (Das & Bal, 2024).

During the alkali extraction step, the hydroxide molecule from the alkali solution reacts with the carrageenan molecules in a somewhat complicated fashion (Mendes et al., 2024). The hydroxyl groups in the alkali solution catalyzes the nucleophilic displacement that causes the formation of an anhydro bonds that cyclizes (adds an additional molecular ring structure) the monomers A content (Campo et al., 2009; Genicot-Joncour et al., 2009). [5] This chemical reaction ultimately liberates sulfate (ultimately reducing the sulfate content) in carrageenan while converting some of monomer A into monomer C, increasing its relative proportion within carrageenan (Mendes et al., 2024).

Additionally, the positively charged ion from the alkali solution reacts with the carrageenan polymers to form a gel (Jouanneau et al., 2010). A gel mechanism involving a coil-to-helix transition and a subsequent step of self-assembling of carrageenan helices is widely acknowledged in the literature (Hilliou, 2021). This mechanism produces the three-dimensional network characteristic of food-grade carrageenans. However, there is currently no consensus among scientists on the network structure responsible for conferring the elasticity properties. The nature of the self-assembling helices is still a source of debate (Hilliou, 2021). There is some evidence that supports the formation of single helices formed by a single carrageenan chain. There is also some evidence that supports the formation of double helices formed by the intertwining of two carrageenan chains (Hilliou, 2021). This gel formation prevents the carrageenan polymers from dissolving into solution and washing away during subsequent washing steps (Mendes et al., 2024). Either way, the presence of ions is essential to the helix formation. The positively charged ions neutralize the charges of sulfate groups and stabilize the helix (Campo et al., 2009). Consequently, these chemical changes also result in a shift of the concentrations of the carrageenan types found in the unprocessed red algae material to the ones present in the food-grade carrageenan (Blakemore, 2016; Blakemore & Harpell, 2010).

Below, we describe changes that occur during the alkali extraction of specific types of carrageenan in more detail.

Kappa-carrageenan's chemical changes during alkali extraction

The carrageenan in unprocessed *Kappaphycus alvarezii* (the primary kappa-carrageenan source) is a random copolymer of (Blakemore, 2016):[6]

a. kappa-carrageenan (70%)
b. mu-carrageenan (30%)

Kappa-carrageenan has a backbone composed of monomers B (4S) and monomers C. Mu-carrageenan has a backbone composed of monomers B (4S) and monomers A (6S) (see *Table 1*). The alkali extraction reaction produces 3,6-anhydrobonds on monomers A (creating an extra molecular ring structure) and one sulfate group on the fourth carbon of monomers B. During the reaction one sulfate group on the sixth carbon of monomers A from mu-carrageenan is removed (Udo et al., 2023). The industrial alkaline extraction has the following consequences (Blakemore, 2016):

a. The mu-carrageenan concentration found in the intermediate carrageenan is reduced from about 30% to about 5%.
b. The kappa-carrageenan concentration increases to about 95% in the final product.

[5] Anhydrobonds are the covalent bonds formed between two molecules by the removal of water.
[6] A random copolymer is a polymer derived from more than one type of monomer where the monomer units are arranged in a random order.

Iota-carrageenan's chemical changes during alkali extraction
Unprocessed iota-carrageenan, mostly extracted from *Eucheuma denticulum*, is also a random copolymer of (Blakemore & Harpell, 2010):

a. iota-carrageenan (70%)
b. nu-carrageenan (30%)

Iota-carrageenan has a backbone composed of monomers B (4S) and monomers C (2S). Nu-carrageenan has a backbone composed of monomers B (4S) and monomers C (2S)(6s) (see *Table 1*). The alkali extraction produces a chemical reaction similar to that described above with the extraction of kappa-carrageenan (Udo et al., 2023). This reaction produces 3,6-anhydrobonds on monomers A. Additionally, it removes sulfate groups on the fourth carbon and second carbon of monomers A and monomers B, respectively. The industrial alkaline extraction yields the following consequences (Blakemore, 2016):

a. reduces the nu-carrageenan content found in the intermediate carrageenan from about 30% to about 5%.
b. iota-carrageenan concentration increases to about 95% to produce the final commercial iota-carrageenan.

Lambda-carrageenan's chemical changes during alkali extraction:
Unprocessed lambda-carrageenan, mostly extracted from *Gigartina* or *Chondrus* species, is a random copolymer of (McKim et al., 2019):

a. lambda-carrageenan (95%)
b. theta-carrageenan (5%)

Positively charged ions, sourced from the alkali solution, have no effect on the non-gelling properties of lambda carrageenan (Blakemore & Harpell, 2010). However, lambda carrageenan will gel in the presence of very high alkali concentrations.

Lambda-carrageenan has a backbone composed of monomers B (2S) and monomers A (2S;6S). Theta-carrageenan has a backbone composed of monomers B (2S) and monomers C (2S) (see *Table 1*). Although commercial lambda-carrageenan does not gel, there is still a chemical change that occurs. Alkaline extraction partially converts the lambda-carrageenan to theta-carrageenan (Udo et al., 2023). The alkaline extraction results in the removal of one sulfate group on the sixth carbon of monomers A during this step. Commercial lambda-carrageenan is ideally comprised of about 90% lambda-carrageenan and 10% theta-carrageenan (Blakemore, 2016).

Poligeenan and degraded carrageenan
Poligeenan is a material the medical community uses as a component of barium sulfate solutions for diagnostic imaging (McKim et al., 2019). Manufacturers create poligeenan by subjecting carrageenan to acid hydrolysis at a pH of 0.9–1.3 at non-physiological temperatures (>80 °C) for several hours (McKim et al., 2019). The resulting liquor is neutralized to approximately pH 7.5. Poligeenan is isolated by roll-drying or spray drying (McKim et al., 2019).

Poligeenan is a low molecular weight molecule (typically 10,000-20,000 Da.).[7] In contrast, refined and semi-refined carrageenan are high molecular weight materials with molecular weights in the range of 200,000–800,000 Da. (Blakemore, 2016; McKim et al., 2019). However, carrageenan can include minor fractions that are below 100,000 Da. and above 800,000 Da. These fractions are naturally occurring and inherent components of the unprocessed red algae material (Blakemore, 2016). These lower molecular weight fractions may also be found in commercial food-grade carrageenan materials and should not be confused with the poligeenan materials that are the products of intentional acid-hydrolysis (McKim et al., 2019).

The term 'degraded carrageenan' describes low molecular weight molecules (20,000-40,000 Da.). This range is slightly higher than the target range for quality poligeenan but still falls within the typical range of the poligeenan molecular weight profile. This material is also the product of acid hydrolysis of carrageenan in the laboratory (McKim et al., 2019). Poligeenan and degraded carrageenan are both part of the poligeenan molecular weight profile. Scientists often referred to degraded-carrageenan in medical experiments from the mid-1950s through the mid-1970s. Scientists during this period were investigating the potential of poligeenan first as an anti-peptic treatment, and then later as an ulcer inducing agent to model gastrointestinal disease (McKim et al., 2019).

In some studies, researchers still use the term carrageenan when describing the use of degraded-carrageenan, which continues to confuse both the scientific community and consumers (McKim et al., 2019; NOP, 2016b). Neither degraded carrageenan nor poligeenan are used as a food additive. However, due to the confusion surrounding these materials, we characterize them here and provide further details about their health implications that have been conflated with carrageenan (see *Evaluation Question #8* below).

[7] This is an abbreviation for Dalton, a common unit of measurement for atomic mass equal to 1/12 the mass of a carbon-12 atom.

Evaluation Question #1(C): Discuss whether this substance is agricultural or nonagricultural. If the substance is nonagricultural, is it synthetic or nonsynthetic (natural) [7 U.S.C. 6502(22); NOP 5033-1 (Decision Tree for Classification of Materials as Synthetic or Nonsynthetic); NOP 5033-2 (Decision Tree for Classification of Agricultural and Nonagricultural Materials for Organic Livestock Production of Handling)]?

Agricultural or nonagricultural classification

Evaluation of carrageenan against Guidance NOP 5033-2 *Decision Tree for Classification of Agricultural and Nonagricultural Materials for Organic Livestock Production or Handling* (NOP, 2016c) is discussed below.

1. *Is the substance a mineral or bacterial culture as included in the definition of nonagricultural substance at section 205.2 of the USDA organic regulations?*

No. Carrageenan is neither a mineral nor a bacterial culture.

2. *Is the substance a microorganism (e.g., yeast, bacteria, fungi) or enzyme?*

No. Carrageenan is a material extracted from red algae.

3. *Is the substance a crop or livestock product or derived from crops or livestock?*

Yes. Carrageenan is derived from the cell wall of red algae, which itself may be farmed or harvested as a wild crop.

4. *Has the substance been processed to the extent that its chemical structure has been changed?*

Yes. During the alkali extraction (or soak) step, the hydroxide molecule from the alkali solution reacts with the carrageenan molecules (Mendes et al., 2024). The hydroxyl groups catalyze the nucleophilic displacement that causes the formation of anhydro bonds (Campo et al., 2009; Genicot-Joncour et al., 2009). This ultimately results in a reduction of the sulfate content and increase the amount of monomer C content in the unprocessed red algal material (Mendes et al., 2024).

Furthermore, the positively charged ions, also from the alkali solution, neutralize the charges of sulfate groups and stabilize the helix (Campo et al., 2009). Consequently, these chemical changes result in a shift of the concentrations of the carrageenan types found in the unprocessed red algae material to the ones present in the food-grade carrageenan (see *Carrageenan's chemical changes during alkali extraction*) (Blakemore, 2016; Blakemore & Harpell, 2010).

5. *Is the chemical change a result of naturally occurring biological processes such as fermentation or use of enzymes; or as a result of mechanical/physical/biological process described under section 205.270(a)?*

No. The chemical change is the result of the introduction of an alkali solution during the manufacture of food-grade carrageenan. Carrageenan can be extracted using hot water; however, the gel strength of materials produced by this method is lower than alkali extracted carrageenan (Tarman et al., 2020). There are alternative extraction methods that could possibly avoid or reduce the usage of solvents (see *Alternative methods of production*) (Rudke et al., 2020; Rupert et al., 2022). Enzyme assisted extraction is another method that researchers have used. Cellulase (an enzyme) is effective in breaking down the fibrous matrix in red algae cell walls and facilitating the release of carrageenan. However, we found no evidence that this method is currently viable beyond research applications. For these reasons, processors generally use alkali extraction for industrial scale production of carrageenan (Tarman et al., 2020).

Therefore, based on the decision tree, carrageenan should be classified as a nonagricultural substance.

Synthetic or nonsynthetic classification

Historic classification of carrageenan, based on the initial classification by the NOSB

During the 1995 NOSB meeting in Orlando, Florida, the NOSB voted to classify carrageenan as nonsynthetic (NOSB, 2009). Prior to the board's vote, a TAP report was conducted that briefly described the manufacturing process for carrageenan (NOSB, 1995). Publicly available notes from the NOSB meeting do not contain any further details regarding the decision to classify carrageenan as nonsynthetic and there are no further details to denote which forms are nonsynthetic. The classification recommended by the NOSB in 1995 was not based on the decision tree in Guidance NOP 5033-1 *Decision Tree for Classification of Materials as Synthetic or Nonsynthetic*, which was not published until 2016 (NOP, 2016a). The 1995 TAP review includes details related to both water and alkali extraction (NOSB, 1995). Based on the NOSB recommendation and the listing of carrageenan on 7 CFR 205.605(a) as nonsynthetic, many certifiers and material review organizations consider carrageenan nonsynthetic.

In 2012, the NOSB Handling committee proposed removing the current listing at § 205.605(a) and adding it to § 205.605(b) (NOSB, 2012a). They cited manufacturing information presented in the 2011 Technical Report to support this proposal (NOP, 2011). The NOSB Handling Subcommittee also proposed that the listing for

carrageenan be revisited once the NOP finalized the guidance that would become NOP 5033 *Classification of Materials* (NOSB, 2012a). Later that same year, the full board reviewed the committee proposal and voted to formally recommended relisting carrageenan at § 205.605(a), but with annotations that (NOSB, 2012b):

- designated the allowed CAS numbers permitted for use as a food processing ingredient (additive)
- prohibited its use in infant formulas

The NOP reviewed the recommendation (78 FR 61154, October 03, 2013). Further, the NOP conducted an independent review that included consultation with the FDA to gain a detailed understanding of the relevant regulations allowing for the use of carrageenan in foods or infant formula. The FDA maintained that carrageenan is safe for use in foods and infant formulas as codified. The NOP noted if the FDA ever changed their position, then it would take appropriate action, if needed, to come into alignment with this finding. Carrageenan was relisted with no change to the annotation (78 FR 61154, October 03, 2013).

In 2016, the NOSB recommended removing carrageenan from § 205.605(a) (NOSB, 2016b). The NOP did not implement the NOSB recommendations because public comments demonstrated that wholly natural substitutes were not available (83 FR 14347, April 04, 2018). In 2021, the NOSB recommended the relisting of carrageenan at § 205.605(a) (NOSB, 2021b).

Classification of carrageenan, using NOP 5033-1

With the exception of direct production of carrageenan from hot water or enzyme assisted extraction, all the manufacturing processes we include in this report are based on the same premise: manufacturers combine red algae with an alkali solution to produce commercial food-grade carrageenan.

Evaluation of carrageenan against Guidance NOP 5033-1 *Decision Tree for Classification of Materials as Synthetic or Nonsynthetic* (NOP, 2016a) is discussed below.

6. Is the substance manufactured, produced, or extracted from a natural source?

Yes. Carrageenan is extracted from the cell wall of red algae, which is a natural material.

7. Has the substance undergone a chemical change so that it is chemically or structurally different than how it naturally occurs in the source material?

Yes. Industrial production methods use alkali treatments to extract a mixture of carrageenan forms from lightly processed red algae. In addition to aiding in the extraction, the alkaline treatment transforms some of the forms of carrageenan (for example, mu- and nu- carrageenan) into different forms (like kappa- and iota-carrageenan). This is a chemical change from how the substance naturally occurs in the source material. Furthermore, the positively charged ions, also from the alkali solution, neutralize the charges of sulfate groups and stabilize the helix formation necessary for gelling (see *Carrageenan's chemical changes during alkali extraction*) (Blakemore, 2016; Blakemore & Harpell, 2010; Campo et al., 2009).

2b. At the end of the extraction process, does the substance meet all the criteria described at 4.6 of NOP 5033?

No. The material has been transformed into a different substance via chemical change as described above.

8. Is the chemical change created by a naturally occurring biological process, such as composting, fermentation, or enzymatic digestion; or, by heating or burning biological matter?

No. While carrageenan can be extracted using hot water, the gel strength of materials produced by this method is lower than alkali extracted carrageenan (Tarman et al., 2020). There are alternative extraction methods that could possibly avoid or reduce the usage of solvents (see *Alternative methods of production*) (Rudke et al., 2020; Rupert et al., 2022). Enzyme assisted extraction is another method that researchers have used. Cellulase (an enzyme) is effective in breaking down the fibrous matrix in red algae cell walls and facilitating the release of carrageenan. However, we found no evidence that this method is currently viable beyond research applications. For these reasons, processors generally use alkali extraction for industrial scale production of carrageenan (Tarman et al., 2020).

Many, if not all, certifiers and material review organizations currently consider carrageenan produced from alkali extraction to be nonsynthetic and therefore the form allowed on the National List at § 205.605(a) (see *Alternative methods of production*). Given that the historic classification of carrageenan produced from alkali extraction may conflict with the outcome of classification using the Guidance NOP 5033-1 *Decision Tree for Classification of Materials as Synthetic or Nonsynthetic* (NOP, 2016a), we note the importance of the NOSB's role in ultimately determining classification and any necessary recommendations to the USDA for regulatory amendments.

Evaluation Question #1(D): Does this substance in its raw or formulated forms contain nanoparticles?
According to NOP Policy Memo 15-2, nanotechnology is conducted at the nanoscale, which is about 1 to 100 nanometers (nm) (NOP, 2015). The NOP uses the term "incidental nanomaterials" to refer to substances that are byproducts of other manufacturing (*e.g.,* homogenization, milling) or that occur naturally (NOP, 2015).

The commercial food-grade carrageenan forms do not contain nanosized particles (with one or more dimensions below 100 nm) (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). The panelists reviewed data submitted on food-grade carrageenan powder and reported that the smallest particles detected in all samples were 300 nm. There are engineered carrageenan forms that may contain nanosized particles. However, these are typically nanocomposites, which are hybrid materials containing mixtures of carrageenan with inorganic solids (*e.g.,* silica or zinc oxide) and are not used as food additives. Engineers develop carrageenan nanocomposites for specific applications in food packaging, controlled drug delivery, and medical procedures (Aga et al., 2021; Manna & Sougata Jana, 2021).

Evaluation Question #1(E): Does this substance in its raw or formulated forms contain ancillary substances?
Manufacturers may include the following ancillary materials in food-grade carrageenan (Cargill, 2017; CP Kelco, 2011; EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018; OMRI, personal communication, August 22, 2025; US Pharmacopeia, 2013):

- sugars for standardization purposes (*e.g.,* dextrose or maltodextrin)
- sodium, potassium, or calcium salts to obtain specific gelling or thickening characteristics
- emulsifiers carried over from drum-drying processes (*e.g.,* xanthan gum)

Food-grade refined carrageenan produced by alcohol precipitation contains approximately 90% anhydrous carrageenan, 8% moisture, and 2% inorganic salts (mainly chlorides) (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). Food-grade refined carrageenan manufactured by the gel-press method contains about 77% anhydrous carrageenan, 8% moisture, and up to 15% inorganic salts (mainly chlorides). Additionally, both food-grade refined and semi-refined carrageenan may not contain more than 0.1% of methanol, ethanol, or propane-2-ol, singly or in combination (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).

The original TAP report notes that some manufacturers use Polysorbate 80 to assist with the drum-drying process (NOSB, 1995). We found no further information indicating the identity of any emulsifiers that processors may use in drum-drying food-grade carrageenan.

Evaluation Question #1(F): Is this substance created using excluded methods?
We found no instances in which carrageenan is produced through excluded methods.

Carrageenan is derived from the cell wall of red algae, which is a biological raw material. However, we found no evidence that red algae are produced through excluded methods at the current time.

Tissue culture is one method of propagation that producers use to cultivate red algae (Sugumaran et al., 2022). In research studies, scientists commonly used *Ascophyllum nodosum* extract, cytokinins, and auxins as biostimulants and plant growth regulators respectively, in tissue culture (Jiksing et al., 2022). However, due to the high production cost, tissue culture is primarily commercially limited to seedling production (Sugumaran et al., 2022). Furthermore, in Policy Memo 13-1 *Cell Fusion Techniques used in Seed Production* the NOP notes that tissue culture is not an excluded method (NOP, 2013).

There is one specific type of tissue culture, protoplast tissue culture, that scientists can combine with protoplast fusion to manipulate the genetics of algae (Jiksing et al., 2022).[8] Scientists isolate protoplasts from a small fragment of algal thallus tissue and culture it to produce uniform algal seedlings, ideal for seedstock. They then induce separate algal protoplasts to fuse using polyethylene glycol or electrically with a cell fusion system (Jiksing et al., 2022). However, this is an area of continuing research, and we found no evidence that red algae producers use these methods commercially at the present time.

Evaluation Question #8: Describe and summarize any reported effects upon human health from use of this substance [7 U.S.C. 6517(c)(1)(A)(i), 7 U.S.C. 6517(c)(2)(A)(i), and 7 U.S.C. 6518(m)(4)].
We found limited evidence that suggests carrageenan consumption may contribute to increased colonic inflammation and ulceration in rodents, human cells in tissue culture, and humans (see *Inflammation and ulceration* below). There is also conflicting evidence that persists regarding the digestive fate of food-carrageenan (see *Degraded carrageenan* below). We found there is limited data currently available related to the toxicology of food-grade carrageenan (see *Toxicology* below). There are low levels of impurities that may be introduced to food-

[8] Protoplasts are living plant cells without a cell wall.

grade carrageenan through the manufacturing process (see *Impurities in carrageenan* below). Recent research also offers limited evidence that carrageenan may contribute some therapeutic effects related to specific pathogens (see *Antiviral and antibacterial effects* below). There is also some conflicting evidence related to carrageenan consumption and metabolic pathways (see *Metabolic effects* below).

Degraded carrageenan

Due to historical use of the term carrageenan when describing the use of degraded carrageenan, which continues to persist in some research today, there is confusion both amongst scientists and consumers regarding the human health impacts of carrageenan (McKim et al., 2019; NOSB, 2016a). However, neither degraded carrageenan nor poligeenan are used as food additives. Earlier in the report, we characterized these materials (see *Poligeenan and degraded carrageenan*) and provided further details about their health implications that have been conflated with carrageenan (see *Inflammation and ulceration* below).

It is well documented in scientific literature that poligeenan and *degraded* carrageenan (a material similar to poligeenan) exhibit harmful gastrointestinal effects, including intestinal ulcerations and cancer (Liu et al., 2021; McKim et al., 2019). Poligeenan and degraded carrageenan are separate and distinct molecules from food-grade refined or semi-refined carrageenan. Further details on this are described in depth within *Evaluation Question #1(B)*. Carrageenans extracted using mild acid hydrolysis methods may also contain lower molecular weight fractions (20–50 kDa) and kappa-carrageenan can contain up to 6.36% low molecular weight fractions (<200 kDa) (Liu et al., 2021).

Researchers are increasingly investigating the effects of physiologically degraded carrageenan. *In vivo*, consumed food is acidified gradually, and the gut emptying begins as soon as a meal is ingested. Following a normal meal the mean time of gastric emptying is approximately three hours and the pH of the gastric contents decreases from about 5 to between 2 and 1.5 (Capron et al., 1996). In experiments with simulated gastric juice, researchers reported only 10% of the gelled kappa-carrageenan sample exposed to the simulated digestion was reduced to a molecular weight <100 kDa (Capron et al., 1996). Fahoum et al. (2017) used a simulated gastric fluid, complete with pepsin and pH adjusted to biological levels, to produce *in vitro* physiologically-digested kappa-, iota-, and lambda-carrageenan. These iota- and lambda- carrageenan materials when introduced to cancerous human colorectal cells mediated cellular changes associated with impaired epithelial barrier functions and induction of inflammation. These cellular changes were dose dependent. The simulated digested carrageenan materials were introduced at levels of 0.5, 0.05, or 0.005 mg/mL (Fahoum et al., 2017). The highest dose at 0.5 mg/mL is equivalent to 0.05%. This is a concentration similar to the level of carrageenan added to commonly consumed processed foods (Liu et al., 2021).

The recovery of carrageenan in mammalian feces contribute to its current classification as an indigestible dietary carbohydrate (David et al., 2018; NOP, 2016b). However, Shen et al. (2026) investigated the *in vitro* simulated digestion and fermentation characteristics of kappa-carrageenan with different molecular weights and its acetylated derivatives. The simulated digestion involved an oral–gastric-small intestine digestive solution that acted upon the kappa-carrageenan at pH levels set in approximation to the related digestive steps. The simulated digestion the researchers used also included an ascending–transverse–descending colon intestinal flora fermentation system assembled with human-derived intestinal flora. The researchers observed that the kappa-carrageenan with different molecular weights and its acetylated derivatives were not digested in the oral–gastric–small intestinal digestion process, but could be fermented by the colonic flora. Furthermore, these materials were mainly degraded in the ascending colon stage (Shen et al., 2026). The digestive fate of food-grade carrageenan remains unclear at the present time. However, there are an increasing number of researchers that are investigating the role of gut bacteria in the digestion of food-grade carrageenan and how these interactions may impact to human health (see *Gastrointestinal effects* below) (Bellanco et al., 2025; Elias Masiques et al., 2025; Han et al., 2025).

Toxicology

We did not find any toxicological studies that raised concerns about carrageenan in humans at the concentrations typically used in food. Based on its toxicological properties, researchers found that carrageenan is typically nontoxic and nonirritating for mammals. The median lethal dose (LD50) values for oral (rat) and skin (rabbit) exposure exceed 5 g/kg bodyweight and 2 g/ kg bodyweight, respectively (Das & Bal, 2024). The 4-h median lethal concentration (LC50) for inhalation (rat) is >0.93 mg/l of air (Das & Bal, 2024).

We found only minor evidence of carrageenan food allergies in the scientific literature. As of 2024, doctors had reported only two individual cases of people experiencing adverse allergic reactions after ingesting carrageenan (Kimilu et al., 2024).

In a literature review of the current research available related to the health impacts of carrageenan, McKim et al. (2019) concluded that there was no evidence to support that carrageenan was carcinogenic, tumorigenic, genotoxic, or a tumor promoter or initiator.

We found limited studies determining the current levels of public exposure to carrageenan. Researchers surveyed 198 people (133 females and 65 males; ages 17-85) in South Florida and found the daily intake of carrageenan typically ranged from 18–30 mg/kg/d (Shah & Huffman, 2003). The highest average intake reported was in people under 30 years of age at 33.73 mg/kg bw/d (standard deviation ±31.61). Researchers in a large scale study (104,139 people) in France more recently reported the median daily intake of total carrageenan at 0.9 mg/kg bw/d (standard deviation 1.2)(Salame et al., 2024). Both of these studies involved self-reported data, a variable that may introduce some degree of bias to the results. The acceptable daily intake (ADI) of carrageenan is still "not specified (Borsani et al., 2021; David et al., 2018)." In their report for the re-evaluation of the safety of food-grade carrageenan, EFSA (2018) concluded that the acceptable daily intake (ADI) for carrageenan (E407) and processed Eucheuma seaweed (E407a) of 75 mg/kg bw per day should be considered temporary. This was in part due to the lack of adequate data available to address the uncertainties as regards the chemistry, the exposure assessment, biological, and toxicological data. The re-evaluation of that temporary ADI has not yet been evaluated at the present time.

Impurities in carrageenan

Processors reported to the EFSA panel that they do not use pesticides in the production of the red algae (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). Documentation provided to the EFSA panel also demonstrated that the presence of pesticides was not detectable (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).

Low levels of formaldehyde are a natural component of most marine algae, including red seaweeds (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). However, processing steps, particularly those involving methanol, may also inadvertently contribute a fraction of formaldehyde to the food-grade carrageenan (Sun et al., 2025). Consequently, formaldehyde may be present as an impurity in food-grade carrageenan (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). However, exposure to formaldehyde from food sources is generally considered negligible because of the high turnover of formaldehyde in the body (878–1310 mg/kg body weight per day) (Sun et al., 2025). Maximum limits for formaldehyde (up to a maximum of 5 mg/kg) are also established in the current EU Regulation legislation for carrageenan (E407) and processed Eucheuma seaweed (E407a) (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). Carrageenan manufacturers do not add formaldehyde during the manufacturing process (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).

Bleaching is an optional step manufacturers may use to produce semi-refined carrageenan. Bleaching can result in the inadvertent production of semicarbazide (Hoenicke et al., 2004).[9] Semicarbazide can occur naturally in marine organisms, including algae, and is formed from naturally occurring biological substances (Hoenicke et al., 2004). Scientists previously observed a weak genotoxic effect exerted by semicarbazide *in vitro* (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018; Hoenicke et al., 2004).[10]

Food-grade, semi-refined carrageenan at a maximum inclusion rate of 2% in processed food formulations with a semicarbazide contribution of 39 µg/kg would add 0.78 µg/kg of the to the final processed food (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). In 2005, manufacturers tested 25 batches of semi-refined carrageenan for semicarbazide and reported a rage of 9–380 µg/kg with a mean of 65 µg/kg. At the mean concentration of 65 µg/kg from use of hypochlorite in the production process, if consumption of carrageenan was up to the advised dietary intake level of 75 mg/kg bodyweight per day the intake of semicarbazide could be as much as 0.005 µg/kg bodyweight per day (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018). However, a large margin of at least 5 orders of magnitude exists between the dose of semicarbazide causing tumors in experimental animals and human exposure. Consequently, the AFC Panel of the EFSA concluded that "the issue of carcinogenicity is not of concern for human health at the concentrations of semicarbazide encountered in food" (EFSA Panel on Food Additives and Nutrient Sources added to Food, 2018).

Inflammation and ulceration

Inflammatory immune responses in cell culture

Evidence from research suggests that carrageenan affects inflammatory pathways in the mammalian digestive system (David et al., 2018; Guo et al., 2023). Scientists have observed the presence of carrageenan may coincide with the triggering of an inflammatory immune response that sometimes also involves the destruction of the cellular mucosal barrier. The underlying mechanisms responsible for these inflammatory effects are unclear at the present time (Han et al., 2025). In a cell culture study, Jiang et al. (2013) demonstrated that treating cancerous human colorectal cells with a combination of kappa-carrageenan and immune cells (macrophages) disrupted the mucosal

[9] Semicarbazide is a protein-bound side-chain metabolite that can occur naturally in algae treated with hypochlorite.

[10] The term *in vitro* indicates that a scientific experiment is done outside the organism, typically on an isolated cell or tissue. The term *in vivo* indicates that scientists conduct the experiment within a living organism.

barrier. The researchers reported that even without carrageenan treatment, the immune cells caused some damage to mucosal barrier of the colorectal cells. The two different cell types were not directly in contact with each other and interacted only via soluble factors secreted from each cell type. Following introduction of the carrageenan treatment, the damage to the mucosal barrier increased significantly. However, a negligible effect was observed when carrageenan was applied to these cell cultures separately (Jiang et al., 2013).

Vissers et al. (2025) observed that kappa-carrageenan caused increased genetic expression of inflammation indicators in intestinal epithelial cells derived from patients with Crohn's disease. The researchers also observed stronger pro-inflammatory effects when inflammation was already present, as it commonly is with people living with inflammatory bowel disease. None of the food-grade carrageenan (kappa-, iota-, and lambda-) altered the permeability of the cells. Disruption of the intestinal barrier is currently recognized as a factor in the initiation of inflammatory bowel disease (Vissers et al., 2025).

Inflammatory immune responses in humans

The pro-inflammatory effects of carrageenan may be particularly important to human populations with distinct digestive profiles, including those living with inflammatory bowel disease. Inflammatory bowel disease, is a general term for chronic diseases of the intestine, such as Crohn's disease and ulcerative colitis (Guo et al., 2023).

Researchers conducted a limited human trial for 12 months to assess if patients with ulcerative colitis in clinical remission would have a longer interval to relapse if they followed a diet with no carrageenan (Bhattacharyya et al., 2017). The study involved a total of 12 patients. Three of the five patients that received carrageenan treatment relapsed. None of the patients that received the placebo treatment relapsed. The amount of carrageenan in the daily treatment was 200 mg, after an initial acclimation period at 100 mg daily. The carrageenan treatment was food-grade and contained equal parts of kappa-, iota-, and lambda-carrageenan. All participants were instructed to follow a carrageenan-free diet. Relapse was defined as an increase of two or more points on a defined disease activity score and intensification of treatment for ulcerative colitis. The researchers also collected data on inflammatory indicators. Bhatacharyya et al. (2017).

Another group of researchers fed mice with induced infectious murine colitis different concentrations of lambda-carrageenan for 90 days and observed mucus layer defects and altered gut bacterial metabolism (Wu et al., 2021). The researchers could reproduce these effects in germ-free mice by fecal transplantation from mice with induced infectious murine colitis fed lambda-carrageenan, but not from germ-free mice only fed lambda-carrageenan (without fecal transplantation). The germ-free mice were raised in a sterile environment without any microorganisms. The researchers concluded that lambda-carrageenan may create an environment that favors inflammation by altering gut microbiota composition and gut bacterial metabolism (Wu et al., 2021).

Researchers recently documented an elevated abundance of *Bacteroides* in human fecal bacteria exposed to food-grade lambda-carrageenan that led to further investigation of the potential utilization of carrageenan by *Bacteroides* (Han et al., 2025). They successfully isolated *B. xylanisolvens C3*, a bacterium that degrades lambda-carrageenan, as demonstrated by their growth using this carrageenan as the sole substrate. The researchers also observed a significant increase of nitric oxide production and inflammation-related gene expression genes (including IL-1β, TNF-α, and IL-6) in mouse macrophage cell culture when the cells were exposed to degraded carrageenan derived from bacterial fermentation by *B. xylanisolvens C3*. From these observations, the researchers concluded that degraded carrageenan derived from bacterial fermentation both activates macrophages and strongly influences macrophage-mediated inflammatory responses. The researchers observed the increase of nitric oxide, but not expression of the inflammation indicators, when they treated the mouse macrophage cell culture with the bacteria *B. xylanisolvens C3* alone, without any bacterially degraded carrageenan. The inflammatory response the researchers observed with the degraded carrageenan derived from bacterial fermentation was similar to the response that the researchers concurrently induced by exposing another group of the macrophage cells to lipopolysaccharides (Han et al., 2025). Lipopolysaccharides are compounds known to stimulate macrophages and trigger significant inflammatory responses.

The intake of carrageenan can lead to changes in the gut microbiota. Bellanco et al. (2025) assessed the impact of food-grade carrageenan on the intestinal barrier. The scientists added carrageenan to a four-stage reactor system that mimicked *in vitro* the ascending, transverse, and descending regions of the colon. This system was stabilized with human fecal microorganisms. The scientists reported an increase in some pro-inflammatory microbial species with increasing doses of carrageenan.[11] The interaction between the carrageenan-fed microorganisms and the intestinal epithelium was assessed *in vitro* using human colorectal cells. They also observed that the changes to the microbiome caused by carrageenan triggered a disruption of the epithelial barrier in a dose-dependent manner. However, neither the undegraded carrageenan, nor the isolated microorganisms alone disrupted the epithelial

[11] Metagenomics is the study of the entire genetic content of all microbiota members in a habitat, such as the simulated digestive system reactor in this experiment.

integrity. These results suggest that microbial metabolites derived from bacterial-generated degradation are responsible for the loss of epithelial integrity. The same research group also found that the intestines of mice that were fed carrageenan had significantly more inflammation than the intestines of mice not fed carrageenan (Bellanco et al., 2025).

In contrast to studies indicating that carrageenan can contribute to gut inflammation, other studies show the opposite. For example, scientists incorporated 1% kappa-carrageenan into pork to investigate the effects on protein digestibility (Elias Masiques et al., 2025). The researchers assessed the protein digestibility and subsequent microbial fermentation metabolites *in vitro* using an enzymatic digestion method simulating the conditions in the mouth, stomach, and small intestine. They also fed rats a diet containing the pork with 1% kappa-carrageenan to assess broader gut and systemic health outcomes after three weeks of dietary intervention (Elias Masiques et al., 2025). The scientists reported the low-fiber pork diet without carrageenan promoted *Akkermansia* and *Tannerellaceae* growth in the colon, while kappa-carrageenan increased *Desulfovibrio* and *Alistipes*. The scientists also observed signs of elevated colonic inflammation (fecal calprotectin and inflammatory pathway indicators) in the rats fed pork without kappa-carrageenan compared to those fed pork prepared with kappa-carrageenan. This inflammation might have resulted from the overgrowth of *Akkermansia* and *Parabacteroides*, known for their mucus-degrading capacity when present in excessive abundance. These diets were intentionally fiber-deprived to mimic typical Western dietary patterns.

Further research is necessary to elucidate the full biochemical relationship between human microbiota and carrageenan and any related consequences on health.

Antiviral and antibacterial effects

There is limited evidence that carrageenan may act as an antiviral and antibacterial agent in some instances. Scientists in multiple *in vitro* and *in vivo* studies found that carrageenan possesses potent and specific inhibitory effects against several viruses, including herpes simplex virus (Das & Bal, 2024). Scientists studied the efficacy of iota-carrageenan as a nasal spray for treating early common cold symptoms in clinical trials. Participants treated with iota-carrageenan experienced a significant reduction in cold symptoms compared to those in the placebo group (Das & Bal, 2024). Inic-Kanada et al. (2018) also observed that iota-carrageenan blocked the ability for the bacteria that causes chlamydia from attaching to the epithelial host cells of guinea pigs. The authors suggested that it might be a promising and affordable therapeutic agent against chlamydial infections in humans (Inic-Kanada et al., 2018).

Metabolic effects

There is some evidence that including carrageenan in the diet may have a positive impact on the maintenance/regulation of lipids (Das & Bal, 2024; Valado et al., 2022). Common parameters of the lipid profile include total cholesterol, low-density lipoprotein cholesterol, triglycerides, and high-density lipoprotein cholesterol. Scientists have studied the effects of carrageenan on the lipid profile of both animal and human models. The conclusions researchers have drawn from these studies are mixed.

In mice, researchers previously observed that exposure to carrageenan in drinking water can lead to glucose intolerance after six days of treatment and produce elevated fasting blood glucose after 23 weeks. This study involved treatment groups exposed to either carrageenan (delivered in water), a high fat diet, or the combination of high fat diet and carrageenan, or no treatment, for one year. The researchers in this study also noted that carrageenan alone had limited impact on the lipid parameters, but the combination of high fat diet and carrageenan significantly increased the non-HDL cholesterol and total cholesterol in the mice (Bhattacharyya et al., 2015). The researchers also observed significant increases in the expression of some inflammatory indicators (IL-6 and MCP-1) in the blood of the mice exposed to treatments containing carrageenan.

In contrast, after analysis of studies in non-human animal models, Valado et al. (2022) concluded that all the studies they reviewed showed a significant reduction in the serum concentration of total cholesterol following a variety of modes of ingestion of carrageenan. The same scientists also analyzed three published studies on humans and also observed carrageenan may impact the regulatory action of the lipid profile (Valado et al., 2022).

Feferman et al. (2020) conducted a limited human trial with 13 human participants with clinical prediabetes that lasted 12 weeks. One treatment group was provided all meals and snacks with no carrageenan. A second treatment group received a similar diet with equivalent content of protein, fat, and carbohydrate, but with carrageenan. The researchers reported significant declines of both HbA1c and HOMA-IR participants on no-carrageenan diets, but not in participants on carrageenan-containing diets. Scientists use these measurements to evaluate insulin signaling and glucose tolerance. The researchers concluded that carrageenan may negatively impact insulin signaling and glucose tolerance. The researchers noted that larger studies are needed to further define these effects (Feferman et al., 2020).

Another group of researchers conducted a limited human trial with 20 human, male participants that lasted two weeks to investigate whether the consumption of carrageenan had an impact on insulin resistance and gut inflammation (Wagner et al., 2024). The daily treatment for the group consuming carrageenan was a capsule containing 250 mg of carrageenan (E407) twice a day. The researchers collected data related to insulin sensitivity, inflammation indicators, intestinal permeability, and gut microbiome composition. They concluded from the data collected that insulin sensitivity did not show significant differences between the treatments. However, the researchers noted that in the overweight participants, the carrageenan exposure resulted in some insulin sensitivity, increased brain inflammation, and elevated expression of inflammatory indicators when compared to the participants with no carrageenan treatment. The researchers also observed an immune response in the white blood cells sourced from the participants after carrageenan exposure. This response involved natural killer cell activation and increased pro-inflammatory cytokine release (Wagner et al., 2024).

Recently, Salame et al. (2024) published a large human health study involving 104,139 participants in France. At the start of the study, and every 6 months thereafter, the participants filled out three non-consecutive days of 24 h dietary records, randomly assigned over a 2-week period. This included two weekdays and one weekend day to account for variability in the diet across the week and the seasons. 1056 of the participants were diagnosed with type 2 diabetes during follow-up for this study (mean follow-up duration 6·8 years). The researchers calculated the exposure to a variety of emulsifiers, including carrageenan, by reviewing the dietary records provided by the participants, multiple food composition databases, and laboratory assays. They then analyzed the associations between cumulative time-dependent exposures to food additive emulsifiers and the risk of type 2 diabetes using statistical methods. The researchers concluded from the data that the consumption of several emulsifiers at the levels documented in the dietary records were associated with an increased risk of type 2 diabetes. In this study, no participant exceeded the ADI of 75 mg/kg bodyweight per day for total carrageenans (E-407–407a). However, the researchers noted a statistically significant, positive association with type 2 diabetes for both total carrageenans (E407+E407a) and carrageenan (E407) (Salame et al., 2024). The researchers noted the strengths of this study includes large sample size and meticulous assessment of dietary exposures. However, there are unmeasured and inherent limitations of self-reported data that may not fully capture the lifestyle and dietary factors of every participant.

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