Carrageenan

1 Nonproprietary Names

USPNF: Carrageenan

2 Synonyms

Chondrus extract; E407; *Gelcarin*; *Genu*; *Hygum TP-1*; Irish moss extract; *Marine Colloids*; *SeaSpen PF*; *Viscarin*.

3 Chemical Name and CAS Registry Number

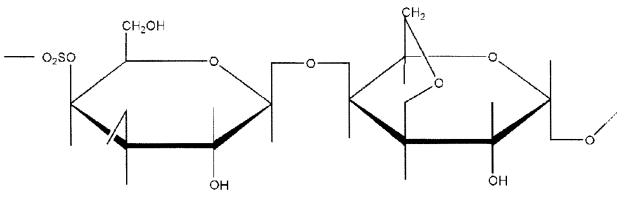
Carrageenan [9000-07-1]
κ-Carrageenan [11114-20-8]
λ-Carrageenan [9064-57-7]

4 Empirical Formula Molecular Weight

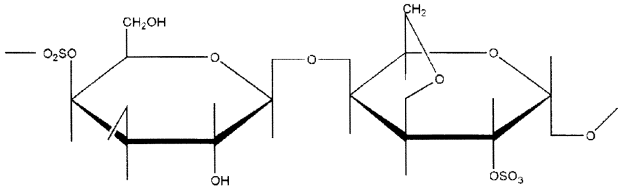
The USPNF 20 describes carrageenan as the hydrocolloid obtained by extraction with water or aqueous alkali from some members of the class Rhodophyceae (red seaweed). It consists chiefly of potassium, sodium, calcium, magnesium, and ammonium sulfate esters of galactose and 3,6-anhydrogalactose copolymers. The sugar units are alternately linked at the α-1,3 and β-1,4 sites.

5 Structural Formula

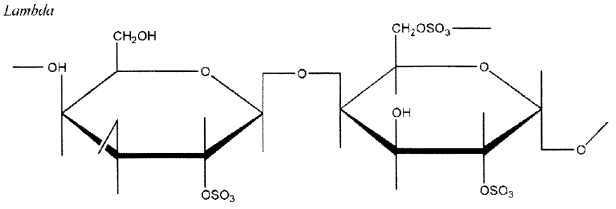
Kappa



Iota



Lambda



As there are three significant types of carrageenan, it is important to distinguish between these structures.

λ-Carrageenan (lambda-carrageenan) is a nongelling polymer containing about 35% ester sulfate by weight and no 3,6-anhydrogalactose.

ι-Carrageenan (iota-carrageenan) is a gelling polymer containing about 32% ester sulfate by weight and approximately 30% 3,6-anhydrogalactose.

κ-Carrageenan (kappa-carrageenan) is a strongly gelling polymer containing 25% ester sulfate by weight and approximately 34% 3,6-anhydrogalactose.

6 Functional Category

Gel base; suspending agent; sustained release tablet matrix.

7 Applications in Pharmaceutical Formulation or Technology

Carrageenan is used in a variety of nonparenteral dosage forms, including suspensions (wet and reconstitutable), topical gels, eye drops, suppositories, and tablets and capsules. In suspension formulations, usually only the ι-carrageenen and λ-carrageenan fractions are used. λ-Carrageenan is generally used at levels of 0.7% w/v or less, and provides viscosity to the liquid.

ι-Carrageenan develops a shear-thinning thixotropic gel, which can be easily poured after shaking. When ι-carrageenan is used, the presence of calcium ions is required for the gel network to become established. With pure ι-carrageenan, about 0.4% w/v is required for most suspensions plus the addition of calcium. However, if *SeaSpen PF* is used, it must be at about 0.75% w/v level, although no additional calcium is required as this is already present in the product to control the rate of gelation.

A study of the effect of carrageenan and other colloids on muco-adhesion of drugs to the oropharyngeal areas[1] concluded that λ-carrageenan had the greatest propensity for adhesion among the fractions studied. λ-Carrageenan exhibits some modification of release of drugs from solution.

The application of carrageenan in both topical gel bases and suppository bases has been examined,[2,3] and the findings indicate that the use of carrageenan in these dosage forms is most likely to be dependent on the active drug, owing to the potential for ionic interactions.

In the case of topical gels, a combination of ι, κ-, and λ-carrageenans produces a spreadable gel with acceptable tactile sensation, resulting in drug release that is more likely to follow diffusion kinetics.

In the case of suppository dosage forms, a greater amount of κ-carrageenan is required in the presence of potassium to form a more rigid structure.

Incorporation of carrageenan into tablet matrices with various drugs and other excipients to alter release profiles has been studied, illustrating that the carrageenans have good tablet-binding properties.[4–6] Furthermore, the inclusion of calcium or potassium salts into the tablet creates a microenvironment for gelation to occur, which further controls drug release.

There have also been several references to the use of carrageenan in chewable tablets having a confectionary texture.[7,8]

This approach to creating a novel dosage form requires the use of both ι-carrageenan and κ-carrageenan, to prevent moisture loss and texture changes that occur over time.

See also Section 10.

8 Description

Carrageenan, when extracted from the appropriate seaweed source, is a yellow-brown to white colored, coarse to fine powder that is odorless and tasteless.

9 Pharmacopeial Specifications

See Table I.

Table I: Pharmacopeial specifications for carrageenan.

Test	USPNF 20
Identification	+
Acid insoluble matter	≤2.0%
Arsenic	≤3 ppm
Heavy metals	≤0.004%
Identification	+
Lead	≤0.001%
Loss on drying	≤12.5%
Total ash	≤35.0%

10 Typical Properties

Because of the vast differences in the material that can be referred to as carrageenan, it is difficult to give descriptions of typical properties. *See* Table II.

Solubility: soluble in water at 80°C. *See* Tables II and III.

Viscosity (dynamic): 5 mPa s (5 cP) at 75°C. *See* Table II.

11 Stability and Storage Conditions

Carrageenan is a stable, though hygroscopic, polysaccharide and should be stored in a cool, dry place; *see* Table II.

12 Incompatibilities

Carrageenan can react with cationic materials. If complexation of cationic materials, with associated modification of the active compound's solubility, is undesirable, the use of carrageenan is not recommended.

Table III: Solubililty and gelation properties of ι-, κ-, and λ-carrageenans.

	Kappa	Iota	Lambda
Solubility			
20°C	Na salt only	Na salt only	Yes
80°C	Yes	Yes	Yes
Gelation			
Ions necessary	K^+	Ca^{2+}	No gel
Texture	Brittle	Elastic	No gel
Re-gelation after shear	No	Yes	—
Acid stability	>pH 3.8	>pH 3.8	—

13 Method of Manufacture

The main species of seaweed from which carrageenan is manufactured are *Eucheuma*, *Chondrus*, and *Gigartina*. The weed is dried quickly to prevent degradation, and is then baled for shipment to processing facilities. The seaweed is repeatedly washed to remove gross impurities such as sand and marine life. The weed undergoes a hot extraction process, releasing the carrageenan from the cell. Once it is in a hot solution, carrageenan undergoes clarification and concentration in solution.

Two processes can be used to remove the carrageenan from solution. The first is a 'freeze–thaw' technique. The solution is gelled with various salts, then the gels are frozen. Upon thawing, the water is removed and the resultant mass, primarily carrageenan and salt, is ground to the desired particle size.

An alternative method, referred to as 'alcohol evaporation' takes the concentrated solution of carrageenan and places it in alcohol. This causes the carrageenan to precipitate out of solution. The cosolvents are evaporated and the precipitated carrageenan is dried and ground to the desired particle size.

14 Safety

Carrageenan is widely used in numerous food applications and is increasingly being used in pharmaceutical formulations. Carrageenan is generally regarded as a relatively nontoxic and nonirritating material when used in nonparenteral pharmaceutical formulations.

However, carrageenan is known to induce inflammatory responses in laboratory animals, and for this reason it is frequently used in experiments for the investigation of anti-inflammatory drugs.[9,10]

Table II: Typical properties of different grades of carrageenan (FMC Biopolymer).

Trade name	Carrageenan type	Gel type	Solubility in water	Viscosity	Use concentration (%)	Use examples
Gelcarin GP-379	Iota	Elastic, medium strength	Hot	High, thixotropic	0.3–1.0	Creams, suspensions
Gelcarin GP-812	Kappa	Brittle, strong	Hot	Low	0.3–1.0	Gels
Gelcarin GP-911	Kappa	Brittle, firm	Hot, partial in cold	Low	0.25–2.0	Encapsulation
SeaSpen PF	Iota	Elastic, weak	Cold, delayed gel formation	Medium, thixotropic	0.5–1.0	Creams, suspensions, lotions
Viscarin GP-109	Lambda	Non-gelling	Partial cold, full in hot	Medium	0.1–1.0	Creams, lotions
Viscarin GP-209	Lambda	Non-gelling	Partial cold, full in hot	High	0.1–1.0	Creams, lotions
Viscarin GP-328	Kappa/lambda	Weak	Hot	Medium–high	0.7–1.2	Creams, emulsions, lotions

The WHO has set an acceptable daily intake of carrageenan of 'not specified' as the total daily intake was not considered to represent a hazard to health.[11] In the UK, the Food Advisory Committee has recommended that carrageenan should not be used as an additive for infant formulas.[12]

LD_{50} (rat, oral): >5 g/kg

15 Handling Precautions

Observe normal precautions appropriate to the circumstances and quantity of material handled.

16 Regulatory Status

GRAS listed. Accepted as a food additive in Europe. Included in the FDA Inactive Ingredients Guide (oral granules, powders and syrups, topical, and transdermal preparations).

17 Related Substances

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18 Comments

The EINECS number for carrageenan is 232-524-2.

19 Specific References

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20 General References

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21 Author

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22 Date of Revision

15 August 2002.