Safety Assessment of Red Algae-Derived Ingredients as Used in Cosmetics

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All interested persons are provided 60 days from the above release date (i.e., May 18, 2020) to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Priya Cherian, Scientific Analyst/Writer.

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1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢
cirinfo@cir-safety.org

INTRODUCTION

The safety of the following 59 red algae ingredients, as used in cosmetics, is reviewed in this assessment.

Ahnfeltiopsis Concinna Extract
Asparagopsis Armata Extract
Betaphycus Gelatinum Extract
Botryocladia Occidentalis Extract
Calliblepharis Ciliata Extract
Ceramium Kondoi Extract
Ceramium Rubrum Extract
Chondracanthus Teedei Powder
Chondrus Crispus
Chondrus Crispus Extract
Chondrus Crispus Powder
Corallina Officinalis Extract
Corallina Officinalis Powder
Corallina Officinalis Thallus Extract
Cyanidium Caldarium Extract
Delesseria Sanguinea Extract
Digenea Simplex Extract
Dilsea Carnosa Extract
Furcellaria Lumbricalis Extract
Gelidiella Acerosa Extract
Gelidium Amansii Extract
Gelidium Amansii Oligosaccharides
Gelidium Cartilagineum Extract
Gelidium Pulchrum Protein
Gelidium Sesquipedale Extract
Gigartina Skottsbergii Extract
Gigartina Stellata Extract
Gloiopeltis Tenax Extract
Gloiopeltis Tenax Powder
Gracilaria Verrucosa Extract
Gracilariopsis Chorda Extract
Grateloupia Livida Powder
Hydrolyzed Asparagopsis Armata Extract
Hydrolyzed Chondrus Crispus Extract
Hydrolyzed Corallina Officinalis
Hydrolyzed Corallina Officinalis Extract
Hydrolyzed Porphyra Yezoensis
Hypnea Musciformis Extract
Lithothamnion Calcareum Extract
Lithothamnion Calcareum Powder
Lithothamnion Corallioides Powder
Mesophyllum Lichenoides Extract
Palmaria Palmata Extract
Palmaria Palmata Powder
Phymatolithon Calcareum Extract
Pikea Robusta Extract
Polysiphonia Lanosa Extract
Porphyra Linearis Powder
Porphyra Tenera Extract
Porphyra Tenera Sporophyte Extract
Porphyra Umbilicalis Extract
Porphyra Umbilicalis Powder
Porphyra Yezoensis Extract
Porphyra Yezoensis Powder
Porphyridium Cruentum Culture Conditioned Media
Porphyridium Cruentum Extract
Porphyridium Purpureum Extract
Rhodymenia Palmata Extract
Sarcodiotheca Gaudichaudii Extract

The majority of the ingredients in this review are extracts and powders derived from one or multiple species of red algae. Although a total of 59 International Nomenclature Cosmetic Ingredient (INCI) names identifying red-algae derived ingredients were found in the web-based *International Cosmetic Ingredient Dictionary and Handbook (*wINCI *Dictionary*; Table 1); several ingredients appear to be equivalent based on the accepted scientific name, as given in the definition (Table 2).[1] Accordingly, the total number of distinct cosmetic ingredients is 56.

According to the *Dictionary*, these red-algae derived ingredients are mostly used as skin-conditioning agents (Table 2).[1] These ingredients are also reported to be used as abrasives, antioxidants, exfoliants, skin protectants, skin bleaching agents, viscosity increasing agents, and anti-microbial agents.

The names of the ingredients in this report are written in accordance with the INCI naming conventions, i.e., capitalized without italics or abbreviations. When referring to the algae from which ingredients are derived, the standard taxonomic practice of using italics is followed (e.g., *Ahnfeltiopsis concinna*). It is often not known how the substance being tested in a study compares to the cosmetic ingredient. In the report text, if it is known that the material being tested is a cosmetic ingredient, the INCI naming convention will be used (e.g., Asparagopsis Armata Extract). However, if it is not known that the test substance is the same as the cosmetic ingredient, the taxonomic naming conventions (e.g., an *Asparagopsis armata* extract) will be used.

Several ingredients that are obtained from red algae, such as agar, carrageenan, hydrolyzed carrageenan, and hydrolyzed furcellaran have been previously reviewed by the Expert Panel for Cosmetic Ingredient Safety (Panel).[2] In 2015, it was concluded that these ingredients were considered safe in the present practices of use and concentration as described in that safety assessment, however, available data were insufficient in determining the safety of hydrolyzed carrageenan in cosmetic products. The full report on these ingredients can be accessed on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients); therefore, information regarding these ingredients will not be included in this report.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically

evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://ewww.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

These red algae-derived ingredients may contain hundreds of constituents, some of which may have the potential to cause toxic effects. In this assessment, the Panel will review the potential toxicity of each of the red algae ingredients as a whole, complex mixture.

CHEMISTRY

Definition

The ingredients in this safety assessment are derived from various species of red algae. "Algae" is not a taxonomic group, but a functional group of convenience.[3] Not all algae should be considered to be plant-like (seaweed; macroalgae). While some algae are seaweed, some are protozoa, and some are unique and belong in other kingdoms. However, these aquatic and oxygenic organisms are all part of the eclectic group called "algae".

Algae Identification

There are several major groups of algae, they are commonly referred to as red algae (*Rhodophyta*), brown algae (*Phaeophyceae*), green algae (*Chlorophyta*), diatoms (*Bacillariophyceae*), chrysophytes (*Chrysophyta*), blue-green algae (*Cyanophyta*), dinoflagellates (*Pyrrhophyta*), and euglenoids (*Euglenophyta*). The various types of algae are arranged by storage products, pigmentation, and cell wall composition.[3] The corresponding subclass, order, family, and genus for each of the red-algae ingredients are presented in Table 3.

Red algae are marine organisms comprised of approximately 6100 species.[4] These algae lack flagella, and range in size from thin films to filamentous membranous forms of 1 m. The color of red algae results from the presence of the pigments phycoerythrin and phycocyanin. Red algae store floridean starch and floridoside, and the cells walls are made up of long-chain polysaccharide agars, carrageenans, and cellulose. General characteristics and the geographic distribution of several specific species of red algae that are included in this report are presented in Table 4.

Physical and Chemical Properties

No physical or chemical properties of these red algae-derived ingredients were found in the published literature, and unpublished data were not submitted.

Method of Manufacture

The methods below are general to the processing of red algae products, and it is unknown if these apply to cosmetic manufacture.

Asparagopsis Armata Extract and Gelidium Cartilagineum Extract

In order to prepare an *Asparagopsis armata* extract, algae was collected and washed in sea water, and then in fresh water to remove epiphytes, sand, and other extraneous matter.[5] Samples were frozen and then ground with a mixer grinder to make a powder. The samples were then extracted in a 1:4 biomass : solvent ratio with methanol and dichloromethane, constantly stirring for 12 hours. Liquid-liquid extraction was also performed for the methanolic fraction, using n-hexane followed by evaporation in a rotary evaporator. Next, the extracts were solubilized in dimethyl sulfoxide (DMSO) at 100 mg/mL. A similar method of manufacturing was reported for a dichloromethane *Plocamium cartilagineum* extract (equivalent to a *Gelidium cartilagineum* extract).[6]

Digenea Simplex Extract

Dried algal powder (200 mg) was extracted with 6 mL 80% methanol in an ultrasonic bath for 30 minutes, vortexed, and then kept at room temperature for 48 hours.[7] After vortexing once more, extracts were centrifuged for 15 minutes, filtered through filter paper, and then dried, to produce a *Digenea simplex* extract.

Gelidiella Acerosa Extract

To prepare a *Gelidiella acerosa* extract, 100 g of the seaweed was packed in a Soxhlet apparatus.[8] Approximately 300 mL of solvent was placed in the solvent reservoir and the extraction was carried out for 6 hours using a wide range of solvents successively (petroleum ether, hexane, benzene, dichloromethane, chloroform, ethyl acetate, acetone, methanol, and water). All extracts were then redistilled to remove solvents from extracts. The extracts were then filtered using filter paper, and kept in a desiccator to remove solvents completely.

Geldium Amansii Extract

To prepare a *Gelidium amansii* extract, the algae was collected and washed three times to remove salt and sand.[9] The algae was then dried at room temperature and ground into a powder. The powder was extracted with 80% ethanol for 24 hours at 40° C, and freeze-dried into a powder.

Gracilariopsis Chorda Extract

To prepare a *Gracilariopsis chorda* extract, seaweed was collected, epiphytes and salts were removed by mechanical washing with fresh water, and dried in the shade at room temperature for one week.[10] Dried samples were then pulverized using a grinder. For extraction, ethanol (95%) was poured into a conical flask containing 2 g of the seaweed powder at a ratio of 0.02 g/mL. The mixture was placed in an orbital shaker at 200 rpm at room temperature, for 24 hours, in the dark. The obtained slurry was centrifuged, and the resulting supernatant was filtered through sterile cotton. The filtrate was then concentrated and dried completely under a steam of nitrogen gas.

Composition

Red algae constituents comprise of approximately 50 - 75% carbohydrates, based on dry weight (DW), and the majority of such constituents are cellulose, xylan, mannan, or agar.[11] Red algae also contain proteins, polyphenols, polysaccharides, minerals, and amino acids.

Cyanidium Caldarium Extract

The major lipids in algae samples of *Cyandium caldarium* include monogalactosyl diglyceride, digalactosyl diglyceride, plant sulfolipid, lecithin, phosphatidyl glycerol, phosphatidyl inositol, and phosphatidyl ethanolamine.[12] The fatty acid composition is variable, but major fatty acids include palmitic acid, oleic acid, linoleic acid, and stearic acid.

Gelidiella Acerosa Extract

A phytochemical analysis was performed on several *Gelidiella acerosa* extracts extracted with solvents of varying polarity (hexane, dichloromethane, ethyl acetate, ethanol, and methanol).[13] Total polyphenols (61.2 µg/100 mg) and flavonoids (13 µg/100 mg) were highest in the ethyl acetate *Gelidiella acerosa* extract.

Gelidium Amansii Extract

The total polyphenolic and flavonoid content of a methanolic *Gelidium amansii* extract was reported to be 0.26 ± 0.08 mg/mL and 1.55 ± 0.16 mg/mL, respectively.[9]

Gloiopeltis Tenax Extract

The essential constituents of *Gloiopeltis tenax* were extracted by supercritical carbon dioxide extraction, and the constituents were identified and analyzed by gas chromatography-mass spectroscopy.[14] The identified constituents included six sesquiterpenes (14.39%), three ketones (5.02%), seven fatty acids and their esters (29.1%), two phenols (1.71%) and three sterols (12.81%). A list of 23 of the constituents identified is provided in Table 5.

Gracilaria Verrucosa Extract

Mycosporine-like amino acids (MAAs) were detected in a crude aqueous *Gracilariopsis longissima* extract (equivalent to *Gracilaria verrucosa* extract) via a high performance chromatography-photodiode array detector and electrospray ionization mass spectrometry.[15] The five MAAs detected include palythine (0.3 ± 0.1%), asterina-330 (42.9 ± 1.1%), shinorine (41.2 ± 2%), porphyra-334 (1.7 ± 0.1%), and palythinol (13.9 ± 0.5%).

Gracilariopsis Chorda Extract

The amount of arachidonic acid in an ethanolic *Gracilariopsis chorda* extract and *Gracilariopsis chorda* powder was determined via reverse-phase high-pressure liquid chromatography.[10] The arachidonic acid content was calculated as 0.64% of the *Gracilariopsis chorda* extract, and 1.5 mg/100 DW of the *Gracilariopsis chorda* powder.

Grateloupia Livida Extract

The chemical composition of a petroleum ether fraction of *Grateloupia livida* was evaluated by gas chromatography-mass spectrometry.[16] The primary constituents detected were n-hexadecanoic acid (20.68%), mono-(2-ethylhexyl) phthalate (11.08%), cholesterol (9.16%), methyl eicosapentaenoate (6.98%), and heptadecane (6.68%).

Hypnea Musciformis Extract

The total phenolic content of a methanolic *Hypnea musciformis* extract was reported to be 6.9 mg gallic acid equivalent (GAE)/g.[17]

Lithothamnion Calcareum Extract

A *Lithothamnion calcareum* extract was reported to contain 12% calcium, 1% magnesium, and measurable levels of 72 other trace minerals, including manganese, selenium, copper, and zinc.[18]

Palmaria Palmata Extract

The total protein content in *Palmaria palmata* has been reported to be in the range of 8-35%, and is variable based on geographical and seasonal variations.[19] The most abundant amino acids in this red algae species are alanine, aspartic acid, glutamic acid, and glycine. Samples of newly dried fresh, as well as stored dry, *Palmaria palmata* were analyzed for their contents of phylloquinone (vitamin K_1). The results indicated that the contents are fairly low (in the range of 2-7 µg/g). In

addition, kainic acid has been reported to be present in *Palmaria palmata* and *Digenea simplex*. In the same study, levels of kainic acid in *Palmaria palmata* samples from Iceland ranged from 1-21 μg/g. The phenolic content in algae extracts are variable depending on extraction methods. The total phenolic content in *Palmaria palmata* extracted with distilled water, 80% methanol, 70% acetone, and 100% methanol was reported to be 31.8, 26.5, 25, and 10.7 mg GAE/g, respectively.[20]

Porphyra Tenera Extract, Porphyra Umbilicalis Extract, and Porphyra Yezoensis Extract

Dried *Porphyra* sp. contains numerous nutrients, including proteins, dietary fibers, polyunsaturated fatty acids, minerals, and vitamins.[21] The dried, raw *Porphyra* sp. contains approximately 40% proteins and 40% carbohydrates, which are mostly derived from the soluble dietary fiber, porphyran. Dried *Porphyra* sp. contains a small amount of lipids (approximately 4%), with eicosapentanoic acid (1200 mg/100 g) and palmitic acid (500 mg/100 g) being the predominant fatty acids. Vitamins and minerals, such as vitamin K (2600 μg/100 g), vitamin C (160 mg/100 g), folate (1200 μg/100 g), vitamin B_{12} (78 μg/100 g), potassium (3100 mg/100 g), and iodine (1400 μg/100 g) are found in dried *Porphyra* sp. A large amount of iron (11 mg/100 g) is also found in these species. *Porphyra* sp. also contain compounds such as polysaccharides (porphyrans; > 40% DW), phycobiliproteins (phycoerythrin and phycocyanin), peptides, MAAs, and phenolic compounds (phlorotannin and taurine).

Impurities

Red algae may accumulate compounds like arsenic and antimony, and toxic metals such as cadmium, lead, mercury, tin, and aluminum.[22] The accumulation of these contaminants is influenced by environmental factors and structural features of the algae. Overall, seven of the red algae species reviewed in this report are authorized as vegetables and condiments in France. These species include *Palmaria palmata*, *Porphyra umbilicalis*, *Porphyra tenera*, *Porphyra yezoensis*, *Chondrus crispus*, *Gracilaria verrucosa*, and *Lithothamnion calcareum*. Maximum allowed toxic minerals and metals have been established by French legislature for these species when used in foods (inorganic arsenic, < 3 mg/kg DW); cadmium, < 0.5 mg/kg DW; mercury, < 0.1 mg/kg DW; lead, < 5 mg/kg DW; tin, < 5 mg/kg DW; and iodine, < 2000 mg/kg DW). Toxic metal and metalloid contents in several edible red algae species based on geographical location is provided in Table 6.[23] The highest amount of arsenic (24 – 50 mg/kg DW) was reported in a *Porphyra* species of red algae (location unknown).

Dried nori (*Porphyra* sp.) samples contained none or trace amounts of inorganic arsenic and total arsenic content.[21] However, dried, and toasted nori contain 2.1 – 21.6 mg of total arsenic/kg DW. In addition, Cadmium was reported to be present in dried *Porphyra* sp. products in concentrations varying from 0.58 – 11 mg/kg of DW.

The concentration levels of 20 metals were analyzed by inductively coupled plasma atomic emission spectroscopy in various dehydrated red seaweed genera (*Chondrus, Gelidium, Palmaria,* and *Porphyra),* from two origins (Asia and Europe).[24] The mean metal content in seaweed samples for the different genera of red algae is presented in Table 7. The highest levels of aluminum (32 mg/kg DW) was detected in *Palmaria*, and the highest content of lead (0.15 mg/kg DW) was detected in *Porphyra*.

Levels of iodine in *Palmaria palmata* can exhibit a wide range of value (10-100 μg/g) depending on location and time of harvest.[19] In one study, iodine levels from *Palmaria palmata* samples from several sources were reported to contain iodine in amounts of 5 μg/g or less. In a different study, the total iodine content of *Palmaria palmata* from Maine was reported to be 72 μg/g.[25] Arsenic content also varies widely based on location and age of the specimen. For example, *Palmaria palmata* (young, whole broad-leaf material) from Maine contained < 0.02 μg/g inorganic arsenic, whereas a granular product produced from older *Palmaria palmata* was found to contain 0.3 μg/g. In the same study, the total amounts of arsenic in *Palmaria palmata* specimens from several locations range from 1-10 μg/g. Levels of cadmium and lead in *Palmaria palmata* from different sources are generally found to be below 1 μg/g.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2020 VCRP survey data, Chondrus Crispus Extract is reported to be used in 381 formulations (306 leave-on formulations, 74 rinse-off formulations, and 1 formulation diluted for bath; Table 8).[26] Hypnea Musciformis Extract is reported to be used in 141 formulations, Corallina Officinalis Extract is reported to be used in 96 formulations, and Palmaria Palmata Extract is reported to be used in 83 formulations. All other in-use ingredients are reported to be used in 55 formulations or less. Concentration of use data are pending as a Council survey is currently in progress. The ingredients not in use according to the VCRP are listed in Table 9.

Several of these ingredients are used in formulations that are near the eye (e.g., Chondrus Crispus Extract in eyeliner, eye shadow, eye lotion, and eye makeup remover), could be incidentally ingested (e.g., Furcellaria Lumbricalis Extract in lipstick), and in formulations that come in contact with mucous membranes (e.g., Chondrus Crispus in bath oils, tablets, and salts and Chondrus Crispus Extract in bubble baths).

Additionally, Chondrus Crispus Powder and Hypnea Musciformis Extract are used in cosmetic sprays and could possibly be inhaled. Chondrus Crispus Powder is reported to be used in fragrance preparations and Hypnea Musciformis Extract is reported to be used in hair sprays. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters >10 µm, with propellant sprays yielding a greater fraction of droplets/particles <10 µm compared with pump sprays.[27,28] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[29,30] Chondrus Crispus, Chondrus Crispus Extract, and Corallina Officinalis Extract were reported to be used in face powders and could possibly be inhaled. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the air.[31-33]

None of the red algae-derived ingredients named in this report are restricted from use in any way under the rules governing cosmetic products in the European Union.[34]

Non-Cosmetic

Several species of red algae (e.g., *Palmaria palmata*) have become established as part of popular international cuisine.[35] According to the US FDA, several red algae species (*Gloiopeltis furcata*, *Porphyra crispata*, *Porphyra deutata*, *Porphyra perforata*, *Porphyra suborbiculata*, *Porphyra tenera*, and *Rhodymenia palmata*) are direct food substances that are generally recognized as safe (GRAS) for human consumption for use as flavor enhancers and flavor adjuvants, when the maximum level in food does not exceed the current good manufacturing practice (cGMP). [21CFR184.1121] Of these red algae species, two are relevant for the purposes of this report (*Porphyra tenera* and *Rhodymenia palmata*). Some red algae species are used in Hawaiian, Irish, or Asian cuisine (e.g., *Ahnfeltiopsis concinna*, *Chondrus crispus*, *Gracilaria verrucosa*, *Palmaria palmata*, *Porphyra* sp.) Other red algae species are used in jellies and as thickeners in food products (e.g., *Gelidiella* and *Gracilaria* sp).[36] A listing of red algae species that are frequently ingested by humans as foods is provided in Table 10.

In addition, red algae species have been used in historical folk medicine. Chinese and Japanese monks used preparations containing *Gelidium amansii* to treat sun stroke and fevers.[36] *Gloiopeltis tenax* has also been reported to be used in China to treat diarrhea and colitis.[14] In Japan and the Mediterranean area, *Gelidium cartilagineum* and *Chondrus Crispus* were used in diarrhea and urinary tract irritation treatment.[36] In the US, a jelly extract of *Chondrus crispus* was recommended for the treatment of cough, diarrhea, dysentery, and gastric ulcers. Extracts of the dried red algae, *Digenea simplex*, was sold by Asian apothecaries by the name of "helminol" to treat ascariasis and oxyuriasis.

Red algae species are still used in present-day holistic medicine for treatment and prevention of various ailments. Some red algae species (e.g., *Gigartina*) have been reported to be used in dietary supplements for immunity-boosting effects.[37] The red algae species*, Lithothamnion calcareum,* is marketed as a nutritional supplement for calcium and minerals in Brazil and other countries due to presence of calcium and magnesium carbonate precipitates in the cell wall.[38] This algae is also used in implants for bone surgery, animal nutrition, fertilizers, and soil treatments. *Gracilariopsis chorda* may be used as a medicinal food to prevent neurological disorders.[10] *Grateloupia livida* is also an edible and medicinal seaweed used to treat sore throat, stomachache, ascariasis, and dysentery.[39] Red algae species such as *Gelidium amansii*, *Gelidium cartilagineum*, and *Gigartina stellata* have been reported to be used in pharmaceutical and industrial preparations due to gelling, water-retention, emulsifying, and other physical properties.[17,36] Several red algae species (e.g. *Chondrus crispus* (Irish moss) and *Gelidiella acerosa*) is widely used for the preparation of carrageenan, agar and for other industrial uses.[13,40]

TOXICOKINETIC STUDIES

No toxicokinetic studies on these ingredients were found in the published literature, and unpublished data were not submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

Grateloupia Livida Extract

The acute oral toxicity of several *Grateloupia livida* extracts (petroleum ether, ethyl acetate, n-butyl alcohol, and aqueous) was evaluated in female mice (20/group; strain not specified).[16] Animals were dosed with 5, 30, 300, or 2000 mg/kg of the extracts. No mortality or severe toxic effects were seen with any extract or dose level. The median lethal dose (LD_{50}) values were expected to be greater than 2000 mg/kg.

Lithothamnion Calcareum Extract

A *Lithothamnion calcareum* aqueous suspension was evaluated for acute oral toxicity in groups of 5 female Wistar rats.[38] One group was treated with the aqueous vehicle and the other was treated with a single 2000 mg/kg dose of the *Lithothamnion calcareum* suspension. The method of oral administration was not stated. Clinical observation of the rats was conducted 5, 15, 30 min, and each hour for 12 hours. The rats were also examined twice a day for an additional 13 days. After 14 days, rats were euthanized and subjected to macroscopic and microscopic necropsy. No signs of toxicity were observed in any of the treated rats.

Subchronic Toxicity Studies

Oral

Lithothamnion Calcareum Extract

A *Lithothamnion calcareum* aqueous suspension was evaluated for oral toxicity in Wistar rats.[38] Rats were divided into five groups: a control group (10 rats/sex/group), two experimental groups (10 rats/sex/group), and two satellite test groups (5 rats/sex/group). The satellite control group received the aqueous vehicle alone while the satellite high-dose group received a dose of 2000 mg/kg. A constant volume of *Lithothamnion calcareum* suspension (1000 or 2000 mg/kg) was administered to the test group to the low and high dose groups, respectively, daily via gavage for 90 days. Following treatment, blood was collected and animals were euthanized. No significant abnormalities in mortality, feces, hair, or behavior were identified in any group. Food intake of groups receiving the test substance was statistically higher than in the control group. Serum creatine levels were increased in female rats treated with 1000 mg/kg of the test substance, and in male and female rats treated with 2000 mg/kg of the test substance. Total serum protein levels decreased in rats treated with 2000 mg/kg of the test substance, and an even greater decrease occurred in the high-dose satellite group. Decreased serum albumin levels were observed in male rats treated with 1000 mg/kg of the test substance and in high-dose male and female rats, with a greater decrease observed in the high-dose satellite group. Some differences were observed in the organ weights of the rats, although gross necropsy and histopathologic evaluation of the same organs revealed no abnormality or significant changes between treated and control groups.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Gelidiella Acerosa Extract

The potential reproductive toxicity of a crude extract of *Gelidiella acerosa* was evaluated in albino rats.[41] In order to prepare the crude extract, *Gelidiella acerosa* was collected and extracted into a 1:1 methanol:methylene chloride solvent system and co-precipitated with polyvinylpyrrolidone (PVP). The co-precipitate was dissolved in distilled water to obtain the 1000 mg/kg dose in 1 mL aliquots. Pregnant rats (5/group) were orally administered (via gavage) either 1 mL vehicle (PVP in distilled water) or 1 mL of the crude extract (PVP co-precipitate) in distilled water, daily, at different stages of gestation (on day 1 only, days 1 - 3, days 4 - 6, or days 7 - 8). On day 14 of gestation, animals were laparotomized, and the number of implantation sites, resorption sites, number of viable embryos, and the gross appearance and number of corpora lutea were observed. Administration of the crude extract did not cause significant ($p > 0.05$) change in any of the parameters evaluated in the animals treated during day 1, days 1 - 3, or days 4 - 6 of gestation. Administration of the crude extract on day 7 - 8 of gestation significantly ($p < 0.01$) reduced the total number of viable implantation sites (by 72%), and significantly ($p < 0.01$) increased the number of resorption sites and post-implantation loss (by 89%). Within the same study, 12 rats were divided into two equal groups, and one received 1 mL of the vehicle/day, and the other 1 mL of the crude extract/day. Administration occurred on days 1 - 7 of gestation. After examination of the number of implantation sites, resorption sites, and viable embryos, animals were sutured, treated locally and subcutaneously with antibiotics, and allowed to recover. Apparent size and distribution of the embryos in the uterine horns were also noted. These animals were re-laparotomized on day 14 of gestation, and the above parameters were recorded. The size, appearance, and color of the implants in treated animals were similar to those of the control; however, a clumping of embryos towards the cervical end of the uterine horns was evident in crude extract-treated rats. Animals were also observed on day 14 of gestation. Control animals had the same number of viable implants on day 14 as on day 8 of pregnancy. All embryos in the treated group on day 14 of gestation were non-viable and resorbing. There was a 100% post-implantation loss in the treated group ($p < 0.001$).

GENOTOXICITY STUDIES

In Vitro

Gelidiella Acerosa Extract

An Ames assay was performed using *Salmonella typhimurium* strains TA98, TA100, and TA1538 in order to evaluate the mutagenic potential of a benzene extract of *Gelidiella acerosa* (250, 500, 1000, 2000, and 4000 µg/plate).[8] Assays were performed with and without metabolic activation. No signs of mutagenicity were observed with or without metabolic activation.

CARCINOGENICITY STUDIES

No carcinogenicity studies on these red algae-derived ingredients were found in the published literature, and unpublished data were not submitted.

ANTI-CARCINOGENICITY STUDIES

Hypnea Musciformis Extract

The effect of an ethanolic *Hypnea musciformis* extract on anthracene-induced mammary carcinogenesis was evaluated in female Sprague-Dawley rats (8/group).[42] Rats in group 1 served as a control. Rats in group 2 and 3 received a single subcutaneous injection of 7,12-dimethylbenz[a]anthracene (DMBA) (25 mg/kg bw) in the mammary gland to develop a mammary carcinoma. Rats in group 3 were also orally administered 200 mg/kg bw/d of *Hypnea musciformis* extract for 16 weeks. Rats in group 4 received 200 mg/kg bw *Hypnea musciformis* extract alone, each day, orally, for 16 weeks. (The method of oral administration was not stated.) At the end of the treatment, animals in group 2 showed decreased weight gain compared to control rats ($p < 0.05$). This effect was not seen in animals in any other group. One hundred percent of animals treated with DMBA alone displayed tumors, however in animals treated with DMBA and *Hypnea musciformis* extract, the incidence of mammary tumors was significantly lower (25%). No tumors were observed in control rats or rats treated with *Hypnea musciformis* extract alone.

Anti-Tumorigenicity

In Vitro

Asparagopsis Armata Extract and Gelidium Cartilagineum Extract

The antitumor potential of methanolic and dichloromethane extracts of *Asparagopsis armata* and *Plocamium cartilagineum* (equivalent to *Gelidium cartilagineum*) was evaluated in human liver cancer (HepG-2) cells via cell viability and cell proliferation studies.[6] For the cell viability and proliferation studies, extracts (1000 µg/mL) were incubated with HepG-2 cells for 24 hours. Both methanolic and dichloromethane extracts of *Asparagopsis armata* presented high cytotoxicity with 11 ± 2.98 and 1.51 ± 0.38 % of HepG-2 live cells, respectively. Potent anti-proliferative activity was also induced by the dichloromethane extracts of *Asparagopsis armata* and *Plocamium cartilagineum*, with 98.56 ± 0.81 and 85.13 ± 1.04 % of cell's proliferation reduction, respectively.

Animal

Porphyra Tenera Powder

The effect of *Porphyra tenera* powder on intestinal tumor incidence was evaluated in Sprague-Dawley rats (10/group).[43] Tumors were induced in all experimental animals via a weekly subcutaneous injection of 1,2-dimethylhydrazine (DMH) for 12 weeks. Experimental animals were fed a dietary seaweed preparation containing 2% *Porphyra tenera* powder, and controls were fed a basic diet. Animals were autopsied 8 weeks after the cessation of the diet and DMH administrations. There was a significant decrease ($p < 0.01$) in the incidence of tumors in rats fed *Porphyra tenera* powder (2/10) versus control animals (8/10).

OTHER RELEVANT STUDIES

Cytotoxicity

Ceramium Virgatum Extract, Corallina Officinalis Extract, Furcellaria Lumbricalis Extract, Gelidium Cartilagineum Extract, Porphyra Linearis Extract, and Gelidium Cartilagineum Extract

The cytotoxic potential of *Ceramium virgatum* extract (equivalent to *Ceramium rubrum* extract), *Corallina officinalis* extract, *Furcellaria lumbricalis* extract, *Plocamium cartilagineum* extract (equivalent to *Gelidium cartilagineum* extract), *Porphyra linearis* extract, and *Mastocarpus stellata* extract (equivalent to *Gigartina stellata* extract), was evaluated using rat skeletal myoblasts (L6-cells).[44] Among all extracts tested, only *Corallina officinalis* showed some weak cytotoxic potential towards the mammalian cells (half maximal inhibitory concentration (IC_{50}) value of 88.6 µg/mL). The remaining extracts had no toxicity at the highest concentration.

Gracilariopsis Longissima Extract

The potential cytotoxicity of a crude aqueous *Gracilariopsis longissima* extract (equivalent to *Gracilaria verrucosa* extract) was also evaluated by a 3-(4,5-dimethylthiazol-2yl)-diphenyl tetrazolium bromide (MTT) assay.[15] This assay was carried out in vitro in three cell lines: murine macrophages of the immune system (RAW264.7), gingival fibroblasts (HGF), and immortalized human keratinocytes (HaCaT). All cell lines were exposed to the extract at concentrations ranging from 0 - 10 mg/mL for 72 hours. No cytotoxicity was observed in either human cell line (HGF or HaCaT) at any concentration, however, significant cytotoxicity was observed in murine tumor cells.

Photoprotective Effects

Porphyra Umbilicalis Extract

A study was performed to assess the photoprotective effects of cosmetic formulations containing *Porphyra umbilicalis*.[45] Four groups of four hairless mice were treated with topical formulations on the dorsum for 5 days as follows: group 1 – control (no treatment); group 2 – application of sunscreen formulation containing only ultraviolet light (UV) filters; group 3 – application of sunscreen formulation with 5% *Porphyra umbilicalis* extract; group 4 – application of the sunscreen formulation with 5% *Porphyra umbilicalis*, 1.5% *Ginkgo biloba*, and vitamins A, E, and C. After application, mice were immobilized and exposed to long-wavelength UV (UVA)/mid-wavelength (UVB) radiation for 28 minutes, which resulted in a cumulative UVB dose of approximately 0.67 J/cm^2. Apoptosis and erythema were evaluated in each group. Immunohistochemical analysis showed that UV radiation caused an increase in the expression of p53 and caspase-3, confirming that the damage caused by UV radiation exposure led to apoptosis. Applications of the test material in groups 2, 3, and 4 resulted in a statistically significant reduction in the expression of p53 and caspase-3, with a more pronounced effect following treatment in group 3 (treatment of sunscreen formulation with *Porphyra umbilicalis* extract). Groups 3 and 4 displayed a statistically significant decrease in erythema values compared with the irradiated control ($p < 0.05$) group.

Anti-Allergic Activity of Porphyran

The effect of porphyran (a major component of *Porphyra tenera* and *Porphyra yezoensis*) on the contact hypersensitivity reaction in female Balb/c mice (10/group) was evaluated.[46] Control and treated groups were given a regular diet for 7 days. On day 7 and 8, mice were administered 2 topical applications of 50 µL of a 5% 2,4,6-trinitrochlorobenzene (TNCB) solution in acetone on shaved abdominal skin. The control and treated groups resumed regular diets, however, the porphyran-treated groups were administered either 0.5, 1, or 2% porphyran in drinking water for the remainder of the test period. The control group was given plain water only. Three days after administration of the TNCB solution, 20 µL of a 1% TNCB solution in acetone was applied to the right ear lobe of each mouse. Twenty-four hours later, the thickness of the ear lobe was measured. Oral administration of porphyran at 2% significantly suppressed ear edema induced by 2,4,6-trinitrochlorobenzene. In addition, it was found that porphyran suppressed the serum level of immunoglobin E and the production of interferon-γ in the challenged ear lobe.

DERMAL IRRITATION AND SENSITIZATION STUDIES

No irritation or sensitization studies on these red algae-derived ingredients were found in the published literature, and unpublished data were not submitted.

SUMMARY

This is a safety assessment of 59 red algae-derived ingredients. However, several of these ingredients are equivalent according to accepted scientific names; accordingly, the number of distinct cosmetic ingredients is 56. The ingredients reviewed in this report are primarily extracts and powders derived from red algae species, and may be derived from the whole plant or a defined part of the plant. These ingredients are mostly reported to function in cosmetics as skin-conditioning agents.

According to 2020 VCRP survey data, Chondrus Crispus Extract had the highest amount of reported uses among the red-algae derived ingredients (381 formulations; 306 leave-on formulations). Hypnea Musciformis Extract, Corallina Officinalis Extract, and Palmaria Palmata Extract were reported to be used in 141, 96, and 83 formulations, respectively. All other in-use ingredients were reported to be used in 55 formulations or less. Concentration of use data are pending as a Council survey is currently in progress.

Several species of red algae have become established as part of popular international cuisine (e.g., *Ahnfeltiopsis concinna*, *Chondrus crispus*, *Gracilaria verrucosa*, *Palmaria palmata*, *Porphyra* sp.). According to the US FDA, *Porphyra tenera* and *Rhodymenia palmata* are direct food substances that are GRAS for human consumption for use as flavor enhancers and flavor adjuvants, when the maximum level in food does not exceed the cGMP. [21CFR184.1121] Several red algae species have historical and present-day use in holistic medicine. Red algae also have industrial uses due to their gelling and emulsifying properties.

The acute oral toxicity potential of multiple *Grateloupia livida* extracts were evaluated in female mice at up to 2000 mg/kg. No toxicity was observed with any extract or dose level. Similarly, no acute oral toxicity was observed in Wistar rats given a single 2000 mg/kg dose of an aqueous *Lithothamnion calcareum* suspension. The same test substance was used in a chronic toxicity study in which Wistar rats were given either 1000 or 2000 mg/kg of the suspension. Serum creatine levels were increased in female rats given 1000 mg/kg of the test substance and in males and females treated with 2000 mg/kg of the test substance. Some differences were observed in the organ weights of the rats, although gross necropsy and histopathologic evaluation of the same organs revealed no abnormality or significant changes between treated and control groups.

The potential reproductive toxicity of a crude extract of *Gelidiella acerosa* (1000 mg/kg/d) was evaluated in female albino rats at different stages of gestation. Administration of the crude extract did not cause significant ($p > 0.05$) change in

any of the parameters evaluated in the animals treated during most gestation periods. However, administration of the crude extract on day 7-8 of gestation significantly ($p < 0.01$) reduced the total number of viable implantation sites (by 72%), and significantly ($p < 0.01$) increased the number of resorption sites and post-implantation loss (by 89%). Within the same study, 12 rats were divided into two equal groups, and one received 1 mL of the vehicle/day, and the other 1 mL of the crude extract/day. Administration occurred on days 1 - 7 of gestation. Animals were allowed to recover after the 7-day administration and were re-laparotomized on day 14 of gestation. The size, appearance, and color of the implants in treated animals were similar to those of the control, however, a clumping of embryos towards the cervical end of uterine horns was evident in crude extract-treated rats. When rats were observed on day 14 of gestation, control animals had the same number of viable implants as on day 8 of pregnancy. All embryos in the treated group on day 14 of pregnancy were non-viable and resorbing. There was a 100% post-implantation loss in the treated group ($p < 0.001$).

An Ames assay was performed using *S. typhimurium* strains TA98, TA100, and TA1538 on a benzene extract of *Gelidiella acerosa* at up to 4000 µg/plate. No signs of mutagenicity were observed at any dose level, with or without metabolic activation.

The effect of an ethanolic *Hypnea musciformis* extract on anthracene-induced mammary carcinogenesis was evaluated in female Sprague-Dawley rats. The test groups were given a subcutaneous injection of DMBA to induce carcinomas, along with 200 mg/kg bw/d of the algae extract, orally. Treatment of the algae extract occurred for 16 weeks. Three groups of control animals were either left untreated, treated with DMBA alone, or treated with *Hypnea musciformis* extract alone. One hundred percent of animals treated with DMBA alone displayed tumors, however in animals treated with DMBA and *Hypnea musciformis* extract, the incidence of mammary tumors was significantly lower (25%). No tumors were observed in control rats or rats treated with *Hypnea musciformis* extract alone.

The anti-tumorigenic potential of methanolic and dichloromethane extracts of *Asparagopsis armata* and *Plocamium cartilagineum* (equivalent to *Gelidium cartilagineum*) was evaluated in HepG-2 cells. Cells were incubated with 1000 µg/mL of the extracts and evaluated for cell viability and proliferation. Both methanolic and dichloromethane extracts of *Asparogopsis armata* presented high cytotoxicity with 11 ± 2.98 and 1.51 ± 0.38 % of HepG-2 live cells, respectively. Anti-proliferative activity of HepG-2 cells was observed in cells treated with dichloromethane extracts of both algae species. In an in vivo study, the effect of *Porphyra tenera* powder on intestinal tumor incidence was evaluated in Sprague-Dawley rats. Tumors were induced in animals via a weekly injection of DMH for 12 weeks, and algae-treated animals received a dietary seaweed preparation containing 2% *Porphyra tenera* powder. Control animals were fed a regular diet. There was a significant decrease ($p < 0.01$) in the incidence of tumors in rats fed *Porphyra tenera* powder (2/10) versus control animals (8/10).

The cytotoxic potential of *Ceramium virgatum* extract (equivalent to *Ceramium rubrum* extract), *Corallina officinalis* extract, *Furcellaria lumbricalis* extract, *Plocamium cartilagineum* extract (equivalent to *Gelidium cartilagineum* extract), *Porphyra linearis* extract, and *Mastocarpus stellata* extract (equivalent to *Gigartina stellata* extract), was evaluated using L6-cells.[44] Among all extracts tested, only *Corallina officinalis* showed some weak cytotoxic potential towards the mammalian cells (half maximal inhibitory concentration (IC_{50}) value of 88.6 µg/mL). The remaining extracts had no toxicity at the highest concentration. An MTT assay was performed using human and tumor cells on a crude aqueous extract of *Gracilariopsis longissima* (equivalent to *Gracilaria verrucosa* extract) at up to 10 mg/mL for 72 hours. No cytotoxicity was observed in either human cell line (HGF or HaCaT) at any concentration, however, significant cytotoxicity was observed in murine tumor cells.

The potential photoprotective effects of cosmetic formulations containing 5% *Porphyra umbilicalis* was evaluated in hairless mice (4 animals/group). After administration of the test substance, animals were exposed to radiation. Control groups were also tested with either no treatment or treatment with sunscreen formulations without *Porphyra umbilicalis*. A more pronounced reduction in the expression of p53 and caspase-3 and decreased erythema values were observed in groups treated with Porphyra umbilicalis compared to the control groups.

The effect of porphyran on the contact hypersensitivity reaction in female Balb/c mice was evaluated. After 7 days of treatment with a regular diet, mice were administered 2 topical applications given on consecutive days of 50 µL of a 5% TNCB solution in acetone on shaved abdominal skin. The control and treated groups resumed regular diets, however, the porphyran-treated groups were administered either 0.5, 1, or 2% porphyran in drinking water for the remainder of the test period. Three days after administration of the TNCB solution, 20 µL of a 1% TNCB solution in acetone was applied to the right ear lobe of each mouse. Twenty-four hours later, the thickness of the ear lobe was measured. Oral administration of porphyran at 2% significantly suppressed ear edema induced by 2,4,6-trinitrochlorobenzene. In addition, it was found that porphyran suppressed the serum level of immunoglobin E and the production of interferon-γ in the challenged ear lobe.

INFORMATION SOUGHT

The CIR is seeking the following information on all the red-algae derived ingredients for use in the resulting safety assessment:

-physical and chemical properties
-method of manufacturing data, specific to cosmetic ingredients
-composition/impurities data, specific to cosmetic ingredients
-oral and dermal chronic toxicity data
-dermal irritation/sensitization data, at or above maximum concentration of cosmetic use

TABLES

Table 1. Red algae INCI names

Ahnfeltiopsis Concinna Extract	Furcellaria Lumbricalis Extract	Palmaria Palmata Powder
Asparagopsis Armata Extract	Gelidiella Acerosa Extract	Phymatolithon Calcareum Extract
Hydrolyzed Asparagopsis Armata Extract	Gelidium Amansii Extract	(equivalent to Lithothamnion Calcareum Extract)
Betaphycus Gelatinum Extract	Gelidium Amansii Oligosaccharides	Pikea Robusta Extract
Botryocladia Occidentalis Extract	Gelidium Cartilagineum Extract	Polysiphonia Lanosa Extract
Calliblepharis Ciliata Extract	Gelidium Pulchrum Protein	Porphyra Linearis Powder
Ceramium Kondoi Extract	Gelidium Sesquipedale Extract	Porphyra Tenera Extract
Ceramium Rubrum Extract	Gigartina Skottsbergii Extract	Porphyra Tenera Sporophyte Extract
Chondracanthus Teedei Powder	Gigartina Stellata Extract	Porphyra Umbilicalis Extract
Chondrus Crispus	Gloiopeltis Tenax Extract	Porphyra Umbilicalis Powder
Chondrus Crispus Extract	Gloiopeltis Tenax Powder	Hydrolyzed Porphyra Yezoensis
Chondrus Crispus Powder	Gracilaria Verrucosa Extract	Porphyra Yezoensis Extract
Hydrolyzed Chondrus Crispus Extract	Gracilariopsis Chorda Extract	Porphyra Yezoensis Powder
Corallina Officinalis Extract	Grateloupia Livida Powder	Porphyridium Cruentum Culture Conditioned Media
Corallina Officinalis Powder	Hypnea Musciformis Extract	Porphyridium Cruentum Extract
Corallina Officinalis Thallus Extract	Lithothamnion Calcareum Extract	(equivalent to Porphyridium Purpureum Extract)
Hydrolyzed Corallina Officinalis	(equivalent to Phymatolithon Calcareum Extract)	Porphyridium Purpureum Extract
Hydrolyzed Corallina Officinalis Extract	Lithothamnion Calcareum Powder	(equivalent to Porphyridium Cruentum Extract)
Cyanidium Caldarium Extract	Lithothamnion Corallioides Powder	Rhodymenia Palmata Extract
Delesseria Sanguinea Extract	Mesophyllum Lichenoides Extract	(equivalent to Palmaria Palmata Extract)
Digenea Simplex Extract	Palmaria Palmata Extract	Sarcodiotheca Gaudichaudii Extract
Dilsea Carnosa Extract	(equivalent to Rhodymenia Palmata Extract)	

Table 2. INCI names, definitions, and functions of the red algae-derived ingredients in this safety assessment[1]

Ingredient	Definition	Function
Ahnfeltiopsis Concinna Extract	Ahnfeltiopsis Concinna Extract is the extract of the alga, *Ahnfeltiopsis concinna*. The accepted scientific name for *Ahnfeltiopsis concinna* is *Gymnogongrus durvillei*.	Skin-Conditioning Agents - Emollient; Skin-Conditioning Agents - Miscellaneous
Asparagopsis Armata Extract	Asparagopsis Armata Extract is the extract of the red alga, *Asparagopsis armata*.	Skin-Conditioning Agents - Miscellaneous
Hydrolyzed Asparagopsis Armata Extract	Hydrolyzed Asparagopsis Armata Extract is the hydrolysate of Asparagopsis Armata Extract derived by acid, enzyme, or other method of hydrolysis.	Skin Protectants
Betaphycus Gelatinum Extract	Betaphycus Gelatinum Extract is the extract of the alga, *Betaphycus gelatinum.*	Skin Bleaching Agents
Botryocladia Occidentalis Extract	Botryocladia Occidentalis Extract is the extract of the alga, *Botryocladia occidentalis*.	Skin-Conditioning Agents - Miscellaneous
Calliblepharis Ciliata Extract	Calliblepharis Ciliata Extract is the extract of the algae, *Calliblepharis ciliate.*	Skin-Conditioning Agents - Miscellaneous
Ceramium Kondoi Extract	Ceramium Kondoi Extract is the extract of the algae, *Ceramium kondoi.*	Skin-Conditioning Agents - Humectant
Ceramium Rubrum Extract	Ceramium Rubrum Extract is the extract of the algae, *Ceramium rubrum*. The accepted scientific name for *Ceramium rubrum* is *Ceramium virgatum*.	Skin-Conditioning Agents – Emollient; Skin-Conditioning Agents - Humectant
Chondracanthus Teedei Powder	Chondracanthus Teedei Powder is the powder obtained from the dried, ground alga, *Chondracanthus teedei.*	Skin-Conditioning Agents - Miscellaneous
Chondrus Crispus	Chondrus Crispus is the material obtained from the whole alga, *Chondrus crispus.*	Exfoliants
Chondrus Crispus Extract	Chondrus Crispus Extract is the extract of the red alga, *Chondrus crispus.*	Humectants; Skin-Conditioning Agents - Miscellaneous
Chondrus Crispus Powder	Chondrus Crispus Powder is the powder obtained from the dried, ground alga, *Chondrus crispus.*	Abrasives
Hydrolyzed Chondrus Crispus Extract	Hydrolyzed Chondrus Crispus Extract is the hydrolysate of Chondrus Crispus Extract derived by acid, enzyme, or other method of hydrolysis	Skin-Conditioning Agents - Miscellaneous
Corallina Officinalis Extract	Corallina Officinalis Extract is the extract of the alga, *Corallina officinalis.*	Skin-Conditioning Agents - Miscellaneous
Corallina Officinalis Powder	Corallina Officinalis Powder is the powder obtained from the dried, ground alga, *Corallina officinalis*	Binders; Dispersing Agents – Nonsurfactant; Viscosity Increasing Agents - Nonaqeuous
Corallina Officinalis Thallus Extract	Corallina Officinalis Thallus Extract is the extract of the thallus of *Corallina officinalis.*	Skin-Conditioning Agents - Miscellaneous
Hydrolyzed Corallina Officinalis	Hydrolyzed Corallina Officinalis is the hydrolysate of the whole plant, *Corallina officinalis* derived by acid, enzyme, or other method of hydrolysis.	Skin-Conditioning Agents - Miscellaneous

Table 2. INCI names, definitions, and functions of the red algae-derived ingredients in this safety assessment[1]

Ingredient	Definition	Function
Hydrolyzed Corallina Officinalis Extract	Hydrolyzed Corallina Officinalis Extract is the hydrolysate of the extract of the alga, *Corallina officinalis,* obtained by acid, enzyme, or other method of hydrolysis.	Not Reported
Cyanidium Caldarium Extract	Cyanidium Caldarium Extract is the extract of the alga, *Cyanidium caldarium.*	Skin-Conditioning Agents - Miscellaneous
Delesseria Sanguinea Extract	Delesseria Sanguinea Extract is the extract of the alga, *Delesseria sanguinea.*	Skin-Conditioning Agents - Miscellaneous
Digenea Simplex Extract	Digenea Simplex Extract is the extract of the alga, *Digenea simplex.*	Not Reported
Dilsea Carnosa Extract	Dilsea Carnosa Extract is the extract of the alga, *Dilsea carnosa.*	Skin Protectants
Furcellaria Lumbricalis Extract	Furcellaria Lumbricalis Extract is the extract of the alga, *Furcellaria lumbricalis.*	Skin-Conditioning Agents - Miscellaneous
Gelidiella Acerosa Extract	Gelidiella Acerosa Extract is the extract of the red alga, *Gelidiella acerosa.*	Skin-Conditioning Agents - Miscellaneous
Gelidium Amansii Extract	Gelidium Amansii Extract is the extract of the alga, *Gelidium amansii.*	Skin-Conditioning Agents - Miscellaneous
Gelidium Amansii Oligosaccharides	Gelidium Amansii Oligosaccharides are oligosaccharides produced by the enzymatic degradation of Agar that is obtained from *Gelidium amansii.*	Skin-Conditioning Agents - Humectant
Gelidium Cartilagineum Extract	Gelidium Cartilagineum Extract is the extract of the alga, *Gelidium cartilagineum.* The accepted scientific name for *Gelidium cartilagineum* is *Plocamium cartilagineum.*	Skin-Conditioning Agents - Miscellaneous
Gelidium Pulchrum Protein	Gelidium Pulchrum Protein is the protein fraction isolated from the alga, *Gelidium pulchrum.*	Skin-Conditioning Agents - Miscellaneous
Gelidium Sesquipedale Extract	Gelidium Sesquipedale Extract is the extract of the alga, *Gelidium sesquipedale.* The accepted scientific name for *Gelidium sesquipedale* is *Gelidium corneum.*	Skin Protectants
Gigartina Skottsbergii Extract	Gigartina Skottsbergii Extract is the extract of the alga, *Gigartina skottsbergii.*	Skin-Conditioning Agents - Miscellaneous
Gigartina Stellata Extract	Gigartina Stellata Extract is the extract of the thallus of the alga, *Gigartina stellata.* The accepted scientific name for *Gigartina stellata* is *Mastocarpus stellatus*	Humectants; Skin-Conditioning Agents - Miscellaneous
Gloiopeltis Tenax Extract	Gloiopeltis Tenax Extract is the extract of the alga, *Gloiopeltis tenax.*	Antifungal Agents; Antimicrobial Agents; Antioxidants
Gloiopeltis Tenax Powder	Gloiopeltis Tenax Powder is the powder obtained from the dried, ground alga, *Gloiopeltis tenax.*	Skin-Conditioning Agents - Miscellaneous
Gracilaria Verrucosa Extract	Gracilaria Verrucosa Extract is the extract of the alga, *Gracilaria verrucosa.* The accepted scientific name for *Gracilaria verrucosa* is *Gracilariopsis longissima.*	Humectants; Skin-Protectants; Skin-Conditioning Agents - Humectant
Gracilariopsis Chorda Extract	Gracilariopsis Chorda Extract is the extract of the alga, *Gracilariopsis chorda.*	Skin-Conditioning Agents - Miscellaneous
Grateloupia Livida Powder	Grateloupia Livida Powder is the powder obtained from the dried, ground alga, *Grateloupia livida.*	Viscosity Increasing Agents - Aqueous
Hypnea Musciformis Extract	Hypnea Musciformis Extract is the extract of the red alga, *Hypnea musciformis*.	Skin-Conditioning Agents - Miscellaneous
Lithothamnion Calcareum Extract	Lithothamnion Calcareum Extract is the extract of the red alga, *Lithothamnion calcareum.* The accepted scientific name for *Lithothamnion calcareum* is *Phymatolithon calcareum.*	Skin-Conditioning Agents - Miscellaneous
Lithothamnion Calcareum Powder	*See Phymatolithon Calcareum Extract*	
Lithothamnion Corallioides Powder	Lithothamnion Corallioides Powder is the powder obtained from the dried, ground alga, *Lithothamnion corallioides.*	Abrasives
Mesophyllum Lichenoides Extract	Mesophyllum Lichenoides Extract is the extract of the alga, *Mesophyllum lichenoides.*	Skin-Conditioning Agents - Miscellaneous
Palmaria Palmata Extract	Palmaria Palmata Extract is the extract of the alga, *Palmaria palmata.*	Skin-Conditioning Agents - Miscellaneous
Rhodymenia Palmata Extract	Rhodymenia Palmata Extract is the extract of the alga, *Rhodymenia palmata.* The accepted scientific name for *Rhodymenia palmata* is *Palmaria palmata*	Antioxidants; Binders; Skin-Conditioning Agents - Emollient
Palmaria Palmata Powder	Palmaria Palmata Powder is the powder obtained from the dried, ground alga, *Palmaria palmata.*	Viscosity Increasing Agents - Aqueous
Phymatolithon Calcareum Extract	Phymatolithon Calcareum Extract is the extract of the alga, *Phymatolithon calcareum.*	Skin-Conditioning Agents - Miscellaneous
Lithothamnion Calcareum Powder	Lithothamnion Calcareum Powder is the powder obtained from the dried, ground red alga, *Lithothamnion calcareum.* The accepted scientific name for *Lithothamnion calcareum* is *Phymatolithon calcareum.*	Abrasives
Pikea Robusta Extract	Pikea Robusta Extract is the extract of the alga, *Pikea robusta.* The accepted scientific name for *Pikea robusta* is *Pikea pinnata.*	Antioxidants; Skin Protectants; Skin-Conditioning Agents - Miscellaneous

Table 2. INCI names, definitions, and functions of the red algae-derived ingredients in this safety assessment[1]

Ingredient	Definition	Function
Polysiphonia Lanosa Extract	Polysiphonia Lanosa Extract is the extract of the alga, *Polysiphonia lanosa.* The accepted scientific name for *Polysiphonia lanosa* is *Vertebrata lanosa.*	Skin-Conditioning Agents - Miscellaneous
Porphyra Linearis Powder	Porphyra Linearis Powder is the powder obtained from the dried, ground alga, *Porphyra linearis.*	Exfoliants
Porphyra Tenera Extract	Porphyra Tenera Extract is the extract of the alga, *Porphyra tenera.* The accepted scientific name for *Porphyra tenera* is *Pyropia tenera.*	Skin-Conditioning Agents - Humectant
Porphyra Tenera Sporophyte Extract	Porphyra Tenera Sporophyte Extract is the extract of the sporophyte of the alga, *Porphyra tenera.* The accepted scientific name for *Porphyra tenera* is *Pyropia tenera.*	Antioxidants; Skin Protectants
Porphyra Umbilicalis Extract	Porphyra Umbilicalis Extract is the extract of the alga, *Porphyra umbilicalis.*	Skin-Conditioning Agents - Miscellaneous
Porphyra Umbilicalis Powder	Porphyra Umbilicalis Powder is the powder obtained from the dried, ground alga, *Porphyra umbilicalis.*	Abrasives; Absorbents; Binders; Colorants; Exfoliants; Viscosity Increasing Agents - Nonaqueous
Hydrolyzed Porphyra Yezoensis	Hydrolyzed Porphyra Yezoensis is the hydrolysate of the alga, *Porphyra yezoensis* derived by acid, enzyme, or other method of hydrolysis.	Hair Conditioning Agents; Skin-Conditioning Agents - Humectant
Porphyra Yezoensis Extract	Porphyra Yezoensis Extract is the extract of the alga, *Porphyra yezoensis.* The accepted scientific name for *Porphyra yezoensis* is *Pyropia yezoensis.*	Skin-Conditioning Agents - Miscellaneous
Porphyra Yezoensis Powder	Porphyra Yezoensis Extract is the extract of the alga, *Porphyra yezoensis.* The accepted scientific name for *Porphyra yezoensis* is *Pyropia yezoensis.*	Viscosity Increasing Agents - Aqueous
Porphyridium Cruentum Culture Conditioned Media	Porphyridium Cruentum Culture Conditioned Media is the growth media removed from cultures of the algae, *Porphyridium cruentum*, after several days of growth.	Antioxidants
Porphyridium Cruentum Extract	*See Porphyridium Purpureum Extract*	
Porphyridium Purpureum Extract	Porphyridium Purpureum Extract is the extract of the alga, *Porphyridium purpureum.*	Skin-Conditioning Agents – Miscellaneous
Porphyridium Cruentum Extract	Porphyridium Cruentum Extract is the extract of the alga, *Porphyridium cruentum.* The accepted scientific name for *Porphyridium cruentum* is *Porphyridium purpureum.*	Skin-Conditioning Agents - Miscellaneous
Rhodymenia Palmata Extract	*See Palmaria Palmata Extract*	
Sarcodiotheca Gaudichaudii Extract	Sarcodiotheca Gaudichaudii Extract is the extract of the alga, *Sarcodiotheca gaudichaudii.*	Antioxidants

Table 3. Taxonomy of red-algae derived ingredients based on currently accepted scientific name[47]

Subclass	Order	Family	Genus	Ingredient (INCI name)
Rhodymeniophycidae	Bonnemaisoniales	Bonnemaisoniaceae	Asparagopsis	Asparagopsis Armata Extract
Rhodymeniophycidae	Bonnemaisoniales	Bonnemaisoniaceae	Asparagopsis	Hydrolyzed Asparagopsis Armata Extract
Rhodymeniophycidae	Gigartinales	Solieriaceae	Betaphycus	Betaphycus Gelatinum Extract
Rhodymeniophycidae	Rhodymeniales	Rhodymeniaceae	Botryocladia	Botryocladia Occidentalis Extract
Rhodymeniophycidae	Gigartinales	Cystocloniaceae	Calliblepharis	Calliblepharis Ciliata Extract
Rhodymeniophycidae	Ceramiales	Ceramiaceae	Ceramium	Ceramium Kondoi Extract
Rhodymeniophycidae	Ceramiales	Ceramiaceae	Ceramium	Ceramium Rubrum Extract
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Chondracanthus	Chondracanthus Teedei Powder
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Chondrus	Chondrus Crispus
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Chondrus	Chondrus Crispus Extract
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Chondrus	Chondrus Crispus Powder
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Chondrus	Hydrolyzed Chondrus Crispus Extract
Rhodymeniophycidae	Corallinales	Corallinaceae	Corallina	Corallina Officinalis Extract
Rhodymeniophycidae	Corallinales	Corallinaceae	Corallina	Corallina Officinalis Powder
Rhodymeniophycidae	Corallinales	Corallinaceae	Corallina	Corallina Officinalis Thallus Extract
Rhodymeniophycidae	Corallinales	Corallinaceae	Corallina	Hydrolyzed Corallina Officinalis Extract
Rhodymeniophycidae	Corallinales	Corallinaceae	Corallina	Hydrolyzed Corallina Officinalis Thallus Extract
Rhodymeniophycidae	Cyanidiales	Cyanidiaceae	Cyanidium	Cyanidium Caldarium Extract
Rhodymeniophycidae	Ceramiales	Delesseriaceae	Delesseria	Delesseria Sanguinea Extract
Rhodymeniophycidae	Ceramiales	Rhodomelaceae	Digenea	Digenea Simplex Extract
Rhodymeniophycidae	Gigartinales	Dumontiaceae	Dilsea	Dilsea Carnosa Extract
Rhodymeniophycidae	Gigartinales	Furcellariaceae	Furcellaria	Furcellaria Lumbricalis Extract
Rhodymeniophycidae	Gelidiales	Gelidiellaceae	Gelidiella	Gelidiella Acerosa Extract
Rhodymeniophycidae	Gelidiales	Gelidiaceae	Gelidium	Gelidium Amansii Extract
Rhodymeniophycidae	Gelidiales	Gelidiaceae	Gelidium	Gelidium Amansii Oligosaccharides
Rhodymeniophycidae	Gelidiales	Gelidiaceae	Gelidium	Gelidium Cartilagineum Extract

Table 3. Taxonomy of red-algae derived ingredients based on currently accepted scientific name[47]

Subclass	Order	Family	Genus	Ingredient (INCI name)
Rhodymeniophycidae	Gelidiales	Gelidiaceae	Gelidium	Gelidium Pulchrum Protein
Rhodymeniophycidae	Gelidiales	Gelidiaceae	Gelidium	Gelidium Sesquipedale Extract
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Gigartina	Gigartina Skottsbergii Extract
Rhodymeniophycidae	Gigartinales	Gigartinaceae	Gigartina	Gigartina Stellata Extract
Rhodymeniophycidae	Gigartinales	Endocladiaceae	Gloiopeltis	Gloiopeltis Tenax Extract
Rhodymeniophycidae	Gigartinales	Endocladiaceae	Gloiopeltis	Gloiopeltis Tenax Powder
Rhodymeniophycidae	Gracilariales	Gracilariaceae	Gracilaria	Gracilaria Verrucosa Extract
Rhodymeniophycidae	Gracilariales	Gracilariaceae	Gracilariopsis	Gracilariopsis Chorda Extract
Rhodymeniophycidae	Halymeniales	Halymeniaceae	Grateloupia	Grateloupia Livida Powder
Rhodymeniophycidae	Gigartinales	Phyllophoraceae	Gymnogongrus	Ahnfeltiopsis Concinna Extract
Rhodymeniophycidae	Gigartinales	Cystocloniaceae	Hypnea	Hypnea Musciformis Extract
Corallinophycidae	Corallinales	Lithothamniaceae	Lithothamnion	Lithothamnion Corallioides Powder
Corallinophycidae	Hapalidiales	Mesophyllumaceae	Mesophyllum	Mesophyllum Lichenoides Extract
Nemaliophycidae	Palmariales	Palmariaceae	Palmaria	Palmaria Palmata Extract
Nemaliophycidae	Palmariales	Palmariaceae	Palmaria	Palmaria Palmata Powder
Corallinophycidae	Corallinales	Lithothamniaceae	Phymatolithon	Lithothamnion Calcareum Extract
Corallinophycidae	Corallinales	Lithothamniaceae	Phymatolithon	Lithothamnion Calcareum Powder
Corallinophycidae	Corallinales	Lithothamniaceae	Phymatolithon	Phymatolithon Calcareum Extract
Rhodymeniophycidae	Gigartinales	Dumontiaceae	Pikea	Pikea Robusta Extract
Rhodymeniophycidae	Ceramiales	Rhodomelaceae	Polysiphonia	Polysiphonia Lanosa Extract
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Linearis Powder
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Tenera Extract
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Tenera Sporophyte Extract
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Umbilicalis Extract
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Umbilicalis Powder
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Hydrolyzed Porphyra Yezoensis
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Yezoensis Extract
Bangiophycidae	Bangiales	Bangiaceae	Porphyra	Porphyra Yezoensis Powder
Porphyridiophyceae	Porphyridiales	Porphyridiaceae	Porphyridium	Porphyridium Cruentum Culture Conditioned Media
Porphyridiophyceae	Porphyridiales	Porphyridiaceae	Porphyridium	Porphyridium Cruentum Extract
Porphyridiophyceae	Porphyridiales	Porphyridiaceae	Porphyridium	Porphyridium Purpureum Extract
Rhodymeniophycidae	Rhodymeniales	Rhodymeniaceae	Rhodymenia	Rhodymenia Palmata Extract
Rhodymeniophycidae	Gigartinales	Solieriaceae	Sarcodiotheca	Sarcodiotheca Gaudichaudii Extract

Table 4. General characteristics and geographic distribution of several red algae species

Species	*Description*	*Distribution/Habitat/Ecology*	*References*
Asparagopsis armata	-pale purplish-red gametophytes, quickly degenerating when removed from water -fronds bushy with cylindrical axis (1mm wide and 200 mm long) -irregularly branched -harpoon-like barbs	-native to southern Australia and New Zealand; now found from the British Isles, the Canary, and Salvage Islands, to Senegal	[47,48]
Calliblepharis ciliata	-flattened, subcartilaginous, purple-red fronds -300 mm long and 20 -70 mm wide -irregularly pinnate -short, cylindrical stipe arises from creeping, branched holdfast	-common in South and West -larger lower intertidal pools and subtidal on stones, maerl, and shells -occasionally abundant on bedrock	[47]
Delesseria sanguinea	-membranous, bright crimson fronds, with cartilaginous, cylindrical, branched stipe, from thickened discoid holdfast -up to 300 mm long -branches bear spirally arranged, leaf-like, ovate-lanceolate blades, each with short stipe and pinnately branched midrib	-on rocks, in deep shady lower intertidal pools and in the subtidal -generally distributed, common	[47]
Dilsea carnosa	-dark red, frequently becoming yellow -thickest of the foliose red algae in the North Atlantic -flattened cartilaginous fronds, arising in groups of small, medium, and large from a thick, discoid holdfast -up to 500 mm long, 250 mm wide	-on rocks in shady pools, lower intertidal on rock and shallow subtidal up to 25 m -usually on rock in kelp forests	[47]
Furcellaria lumbricalis	-cartilaginous, cylindrical, brownish-black fronds -repeatedly dichotomously branched -up to 2 mm diameter, 300 mm long, with acute apices	-on rocks, lower intertidal and shallow subtidal -in pools and runnels -in open situations, often on sandy and muddy shores -common, widespread	[47]
Gelidiella acerosa	-thallus yellow to dark red -cartilaginous with decumbent and erect terete axes up to 2 mm diameter -lateral branches, 1-3 mm long	-widespread in most warm seas, just below intertidal zone -attached to rock reefs at depths of 0-1 m	[47]
Phymatolithon calcareum	-fragile, reddish-violet, branched, calcareous fronds -branches are 2-3 mm in diameter -variable in form	-free-living in clear, clean water, forming extensive beds of live and dead material, particularly where there are subtidal currents -widely distributed	[47]
Palmaria palmata	-reddish-brown, membranous or leathery, flattened fronds (50-300 mm long) -blade variable in shape, having broadly ovate to narrowly linear segments -palmate branching with finger-like extensions	-North Atlantic -on rock and mussels, intertidal and shallow subtidal -widely distributed	[47]
Polysiphonia lanosa	-cartilaginous, cylindrical, densely tufted, dark brown fronds up to 75 mm long -repeatedly pseudo dichotomous branches, apices pointed, widely forked	-hemiparasitic on *Ascophyllum nodosum*, more rarely on *Fucus vesiculosus* -never directly on rock -sheltered mid-tidal -generally distributed	[47]
Porphyra linearis	-delicate, linear, membranous, purple-brown fronds, 20-40 mm long and 5-10 mm broad -usually simple with short stipe with basal holdfast -orange patches when reproductive	-zone-forming on rock in the intertidal and splash zone of semi-exposed and exposed shores -generally distributed -winter occurrence	[47]
Sarcodiotheca Gaudichaudii	-medium to large species with cylindrical, brittle fronds -color varies from straw yellow to deep red or reddish brown	-lower intertidal pools to upper subtidal -mainly on small stones and shells	[47]

Table 5. Chemical composition of a supercritical carbon dioxide extract of Gloiopeltis tenax[14]

Constituents	*%**
p-hydroxybenzaldehyde	0.57
(-) – thujopsene	4.68
α-curcumene	1.54
α-zingiberene	2.98
(+)-cuparene	0.28
(−)-β-bisabolene	1.00
cedrol	3.91
vanillylacetone	1.92
n-heptadecane	10.30
myristic acid	2.85
fitone	2.53
methhyl hexadecanoate	1.32
palmitic acid	21.21
linoleic acid	0.23
hexadeca-1,4-lactone	0.57
cis-9-octadecenoic acid	0.73
stearic acid	0.93
oleamide	0.24
2,2′-methylenebis(6-tert-butyl-4-methylphenol)	1.14
2-monopalmitin	1.83
cholesta-4,6-dien-3β-ol	6.62
cholesterol	5.74
cholesta-3,5-dien-7-one	0.45

*percentage of relative amount to total

Table 6. Metalloid and toxic metal content in some edible red algae species in different locations (mg/kg DW)[23]

Species	*Location*	*Arsenic*	*Inorganic Arsenic*	*Cadmium*	*Lead*	*Mercury*	*Antimony*	*Tin*	*Strontium*	*Aluminum*
Chondrus crispus	Unknown	4 - 26	0.2	0.3 - 1	0.1 - 5	0.006	-	3	83	8 - 120
Gracilaria sp.	Greece	-	-	0.8 - 3	10 - 19	-	-	-	-	-
	Italy	15	-	0.04 - 0.4	0.8 - 7	-	-	-	-	19- 149
Palmaria palmata	Spain	15	-	0.1 - 0.3	0.5	-	0.01	-	31	62
	Norway	10	-	0.5	-	0.005	-	-	-	-
	Denmark	8	0.3	< 1	< 1	< 0.005	-	-	-	-
	Iceland	1	< 0.03	< 1	< 1	< 1	-	-	-	-
	Unknown	8 - 10	0.4	0.2 - 0.7	0.05 – 4	0.01	-	1	3 - 71	32-120
Porphyra sp.	Portugal	-	-	0.4 - 1	0.1 - 0.2	< 0.005	-	-	-	-
	Spain	9 - 19	0.1 - 0.6	0.1 - 3	0.3 - 0.5	0.008 - 0.03	0.01 - 0.02	-	2 - 130	15 - 890
	France	4	-	3	0.3		0.03	-	120	22
	Unknown	24 - 50	0.1 - 0.6	0.2 - 4	0.01 - 2	- 0.004 - 0.03	-	<1	25	< 120

- = None reported; DW = dry weight

Table 7. Mean metal content ± standard deviation in seaweed samples for different genera of red algae (mg/kg DW)[24]

	Chondrus (n = 2)	*Gelidium* (n = 2)	*Palmaria* (n = 4)	*Porphyra* (n = 10)
Sodium	6799 ± 84.6	1279 ± 0	3803 ± 463	2274 ± 675
Potassium	9901 ± 270	543 ± 53.2	8044 ± 0	6563 ± 854
Calcium	2028 ± 153	908 ± 7.01	459 ± 0.00	1793 ± 1211
Magnesium	3134 ± 45.7	452 ± 4.68	787 ± 87.6	3732 ± 5070
Boron	43.3 ± 6.60	4.50 ± 0.98	31.5 ± 6.45	5.10 ± 0.00
Barium	0.35 ± 0.08	0.30 ± 0.10	0.62 ± 0.28	3.19 ± 2.88
Cobalt	0.13 ± 0.01	0.008 ± 0.00	0.03 ± 0.01	0.12 ± 0.18
Chromium	0.15 ± 0.00	0.16 ± 0.001	0.15 ± 0.02	0.33 ± 0.14
Copper	0.79 ± 0.21	0.54 ± 0.02	1.03 ± 0.09	2.99 ± 0.68
Iron	22.3 ± 3.79	9.86 ± 0.24	34.7 ± 8.10	156 ± 239
Lithium	0.85 ± 0.01	0.93 ± 0.58	1.16 ± 0.45	1.41 ± 0.00
Manganese	9.78 ± 0.56	1.66 ± 0.01	1.62 ± 0.45	36.5 ± 56.9
Molybdenum	0.12 ± 0.01	0.008 ± 0.00	0.09 ± 0.01	0.22 ± 0.09
Nickel	5.08 ± 0.10	0.11 ± 0.001	0.05 ± 0.13	0.50 ± 0.87
Strontium	-	-	3.44 ± 0.36	2.22 ± 2.92
Vanadium	0.58 ± 0.47	-	25.5 ± 0.00	0.48 ± 0.41
Zinc	9.33 ± 2.57	2.21 ± 0.25	5.03 ± 1.06	13.6 ± 3.72
Aluminum	8.41 ± 2.85	8.21 ± 0.61	32 ± 5.18	28.9 ± 27.3
Cadmium	0.29 ± 0.03	0.008 ± 0.00	0.16 ± 0.11	0.58 ± 0.30
Lead	0.07 ± 0.00	0.05 ± 0.01	0.05 ± 0.02	0.15 ± 0.21

- = None reported

Table 8. Frequency (2020) and concentration of use of red algae-derived ingredients[26]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Ahnfeltiopsis Concinna Extract		**Asparagopsis Armata Extract**		**Chondrus Crispus**	
Totals*	**16**	**NS**	**42**	**NS**	**26**	**NS**
Duration of Use						
Leave-On	*15*	*NS*	*36*	*NS*	20	*NS*
Rinse-Off	*1*	*NS*	*6*	*NS*	4	*NS*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NS*	2	*NS*
Exposure Type						
Eye Area	1	NS	16	NS	4	NS
Incidental Ingestion	NR	NS	NR	NS	4	NS
Incidental Inhalation-Spray	6[a]; 6[b]	NS	7[a]; 8[b]	NS	5[a]; 6[b]	NS
Incidental Inhalation-Powder	6[a]	NS	7[a]	NS	1; 5[a]	NS
Dermal Contact	16	NS	40	NS	22	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	NR	NS	2	NS	NR	NS
Hair-Coloring	NR	NS	NR	NS	NR	NS
Nail	NR	NS	NR	NS	NR	NS
Mucous Membrane	NR	NS	1	NS	6	NS
Baby Products	NR	NS	NR	NS	NR	NS

	Chondrus Crispus Extract		**Chondrus Crispus Powder**		**Corallina Officinalis Extract**	
Totals*	**381**	**NS**	**55**	**NS**	**96**	**NS**
Duration of Use						
Leave-On	*306*	*NS*	49	*NS*	76	*NS*
Rinse Off	*74*	*NS*	6	*NS*	20	*NS*
Diluted for (Bath) Use	*1*	*NS*	NR	*NS*	NR	*NS*
Exposure Type						
Eye Area	60	NS	9	NS	5	NS
Incidental Ingestion	14	NS	NR	NS	1	NS
Incidental Inhalation-Spray	107[a]; 69[b]	NS	1; 25[a]; 9[b]	NS	16[a]; 31[b]	NS
Incidental Inhalation-Powder	21; 107[a]	NS	25[a]	NS	2; 16[a]	NS
Dermal Contact	344	NS	53	NS	81	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	21	NS	2	NS	1	NS
Hair-Coloring	1	NS	NR	NS	NR	NS
Nail	NR	NS	NR	NS	13	NS
Mucous Membrane	21	NS	1	NS	1	NS
Baby Products	NR	NS	NR	NS	NR	NS

Table 8. Frequency (2020) and concentration of use of red algae-derived ingredients[26]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Delesseria Sanguinea Extract		**Digenea Simplex Extract**		**Furcellaria Lumbricalis Extract**	
Totals*	**2**	**NS**	**1**	**NS**	**32**	**NS**
Duration of Use						
Leave-On	*2*	*NS*	*NR*	*NS*	*32*	*NS*
Rinse-Off	*NR*	*NS*	*1*	*NS*	*NR*	*NS*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NS*	*NR*	*NS*
Exposure Type						
Eye Area	NR	NS	NR	NS	NR	NS
Incidental Ingestion	NR	NS	NR	NS	2	NS
Incidental Inhalation-Spray	1[a]; 1[b]	NS	NR	NS	9[a]; 11[b]	NS
Incidental Inhalation-Powder	1[a]	NS	NR	NS	9[a]	NS
Dermal Contact	2	NS	1	NS	30	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	NR	NS	NR	NS	NR	NS
Hair-Coloring	NR	NS	NR	NS	NR	NS
Nail	NR	NS	NR	NS	NR	NS
Mucous Membrane	NR	NS	NR	NS	2	NS
Baby Products	NR	NS	NR	NS	NR	NS

	Gelidium Cartilagineum Extract		**Gelidiella Acerosa Extract**		**Gigartina Stellata Extract**	
Totals*	**37**	**NS**	**19**	**NS**	**9**	**NS**
Duration of Use						
Leave-On	*35*	*NS*	*9*	*NS*	*3*	*NS*
Rinse-Off	*2*	*NS*	*10*	*NS*	*6*	*NS*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NS*	*NR*	*NS*
Exposure Type						
Eye Area	3	NS	1	NS	1	NS
Incidental Ingestion	NR	NS	NR	NS	NR	NS
Incidental Inhalation-Spray	16[a]; 14[b]	NS	1[a]; 6[b]	NS	1[a]; 1[b]	NS
Incidental Inhalation-Powder	1; 16[a]	NS	1[a]	NS	NR	NS
Dermal Contact	37	NS	8	NS	3	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	NR	NS	7	NS	6	NS
Hair-Coloring	NR	NS	4	NS	NR	NS
Nail	NR	NS	NR	NS	NR	NS
Mucous Membrane	NR	NS	NR	NS	NR	NS
Baby Products	1	NS	NR	NS	NR	NS

	Hydrolyzed Corallina Officinalis Extract		**Hypnea Musciformis Extract**		**Lithothamnion Calcareum Extract**	
Totals*	**9**	**NS**	**141**	**NS**	**22**	**NS**
Duration of Use						
Leave-On	*6*	*NS*	*75*	*NS*	*22*	*NS*
Rinse-Off	*3*	*NS*	*66*	*NS*	*NR*	*NS*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NS*	*NR*	*NS*
Exposure Type						
Eye Area	1	NS	16	NS	4	NS
Incidental Ingestion	NR	NS	NR	NS	NR	NS
Incidental Inhalation-Spray	4[a]; 1[b]	NS	4; 7[a]; 27[b]	NS	3[a]	NS
Incidental Inhalation-Powder	4[a]	NS	7[a]	NS	3[a]	NS
Dermal Contact	9	NS	73	NS	7	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	NR	NS	34	NS	NR	NS
Hair-Coloring	NR	NS	27	NS	NR	NS
Nail	NR	NS	5	NS	15	NS
Mucous Membrane	1	NS	1	NS	NR	NS
Baby Products	NR	NS	NR	NS	NR	NS

Table 8. Frequency (2020) and concentration of use of red algae-derived ingredients[26]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Lithothamnion Calcareum Powder		**Palmaria Palmata Extract**		**Phymatolithon Calcareum Extract**	
Totals*	**11**	**NS**	**83**	**NS**	**1**	**NS**
Duration of Use						
Leave-On	*2*	*NS*	*75*	*NS*	*1*	*NS*
Rinse-Off	*9*	*NS*	*8*	*NS*	*NR*	*NS*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NS*	*NR*	*NS*
Exposure Type						
Eye Area	NR	NS	8	NS	1	NS
Incidental Ingestion	NR	NS	NR	NS	NR	NS
Incidental Inhalation-Spray	1[a]	NS	30[a]; 22[b]	NS	NR	NS
Incidental Inhalation-Powder	1[a]	NS	30[a]	NS	NR	NS
Dermal Contact	11	NS	83	NS	1	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	NR	NS	NR	NS	NR	NS
Hair-Coloring	NR	NS	NR	NS	NR	NS
Nail	NR	NS	NR	NS	NR	NS
Mucous Membrane	NR	NS	7	NS	NR	NS
Baby Products	NR	NS	NR	NS	NR	NS

	Porphyra Umbilicalis Extract		**Porphyra Yezoensis Extract**		**Porphyridium Cruentum Extract**	
Totals*	**42**	**NS**	**10**		**47**	**NS**
Duration of Use				**NS**		
Leave-On	*35*	*NS*	*8*		*40*	*NS*
Rinse-Off	*7*	*NS*	*2*	*NS*	*7*	*NS*
Diluted for (Bath) Use	*NR*	*NS*	*NR*	*NS*	*NR*	*NS*
Exposure Type				*NS*		
Eye Area	3	NS	1		11	NS
Incidental Ingestion	NR	NS	NR	NS	NR	NS
Incidental Inhalation-Spray	20[a]; 8[b]	NS	3[a]; 4[b]	NS	11[a]; 11[b]	NS
Incidental Inhalation-Powder	20[a]	NS	3[a]	NS	11[a]	NS
Dermal Contact	40	NS	10	NS	47	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair - Non-Coloring	2	NS	NR	NS	NR	NS
Hair-Coloring	NR	NS	NR	NS	NR	NS
Nail	NR	NS	NR	NS	NR	NS
Mucous Membrane	4	NS	NR	NS	NR	NS
Baby Products	NR	NS	NR	NS	NR	NS

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

[a] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

[b] It is possible these products are sprays, but it is not specified whether the reported uses are sprays

[c] It is possible these products are powders, but it is not specified whether the reported uses are powders

NR – no reported use

NS – A concentration of use survey is currently in progress

Table 9. Red algae-derived ingredients with no reported uses in the VCRP

Hydrolyzed Asparagopsis Armata Extract	Gracilaria Verrucosa Extract
Betaphycus Gelatinum Extract	Gracilariopsis Chorda Extract
Botryocladia Occidentalis Extract	Grateloupia Livida Powder
Calliblepharis Ciliata Extract	Lithothamnion Corallioides Powder
Ceramium Kondoi Extract	Mesophyllum Lichenoides Extract
Ceramium Rubrum Extract	Palmaria Palmata Powder
Chondracanthus Teedei Powder	Pikea Robusta Extract
Hydrolyzed Chondrus Crispus Extract	Polysiphonia Lanosa Extract
Corallina Officinalis Powder	Porphyra Linearis Powder
Corallina Officinalis Thallus Extract	Porphyra Tenera Extract
Hydrolyzed Corallina Officinalis	Porphyra Tenera Sporophyte Extract
Cyanidium Caldarium Extract	Porphyra Umbilicalis Powder
Dilsea Carnosa Extract	Hydrolyzed Porphyra Yezoensis
Gelidium Amansii Extract	Porphyra Yezoensis Powder
Gelidium Amansii Oligosaccharides	Porphyridium Cruentum Culture Conditioned Media
Gelidium Pulchrum Protein	Porphyridium Purpureum Extract
Gelidium Sesquipedale Extract	(equivalent to Porphyridium Cruentum Extract)
Gigartina Skottsbergii Extract	Rhodymenia Palmata Extract
Gloiopeltis Tenax Extract	(equivalent to Palmaria Palmata Extract)
Gloiopeltis Tenax Powder	Sarcodiotheca Gaudichaudii Extract

Table 10. Red algae species ingested by humans as foods

Species	Methods of consumption	Reference
Ahnfeltiopsis concinna	Hawaiian cuisine; Eaten raw with limpets or baked with other foods	[49]
Chondrus crispus	Used as thickener/gelling agent; used in drinks; also known as Irish moss; eaten whole	[50]
Gelidiella sp.	Used in jellies	[36]
Gelidium amansii	Used in jellies	[9]
Gigartina stellata	Used interchangeably with Chondrus crispus; thickener/gelling agent	[36,47]
Gracilaria sp.	Used in jellies	[36]
Gracilaria verrucosa	Eaten whole, with salads	[50]
Palmaria palmata	Eaten fresh or dry	[35]
Porphyra tenera	Typically, dried and used to make sushi; spices, seasoning, flavoring (GRAS)	21CFR184.1121, [21]
Porphyra umbilicalis	Typically, dried and used to make sushi	[50]
Porphyra yezoensis	Typically, dried and used to make sushi	[21,51]
Rhodymenia palmata	Spices, seasoning, flavoring (GRAS)	21CFR184.1121

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