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

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ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of red algae-derived ingredients. Sixty red algae-derived ingredients were found in the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*); however, several of these ingredients may be equivalent according to accepted scientific names. These ingredients are mostly reported to function in cosmetics as skin-conditioning agents. Impurities, particularly arsenic, heavy metals, and pesticides, may be present in these ingredients; industry should continue to use good manufacturing practices to monitor and limit these possible impurities. The Panel considered the available data and concluded that 16 red algae-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment. The Panel also concluded that the data are insufficient to make a determination of safety that the remaining 44 ingredients are safe under the intended conditions of use in cosmetic formulations.

INTRODUCTION

The safety of the following 60 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
Kappaphycus Alvarezii 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 different species of red algae. Although a total of 60 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*) several ingredients appear to be equivalent based on the accepted scientific name, as given in the definition.[1] Accordingly, the total number of distinct cosmetic ingredients is 56.

According to the *Dictionary*, these red algae-derived ingredients are mostly reported to function in cosmetics as skin-conditioning agents (Table 1).[1] These ingredients are also reported to function as abrasives, antioxidants, exfoliants, skin protectants, skin bleaching agents, viscosity increasing agents, and anti-microbial agents. It should be noted that some of these reported functions (e.g., skin bleaching and anti-microbial agents) are not considered a cosmetic function in the United States (US), and therefore, use as such does not fall under the purview of the Expert Panel for Cosmetic Ingredient Safety (Panel).

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).

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. Thus, in this assessment, the Panel will assess the safety of each of these red algae-derived ingredients as a whole, complex mixture; toxicity from single components may not predict the potential toxicity of botanical ingredients.

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.

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, 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*). It should be noted that the red algae-derived ingredients reviewed in this report are a part of the *Rhodophyta* phylum; red algae should not be confused with members of the *Pyrrhophyta* phylum, which encompass the unicellular algae and protozoa responsible for harmful algal blooms, known as "red tide." 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 2.

Red algae are of the kingdom Plantae, and are 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 3.

Chemical Properties

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

Method of Manufacture

Numerous methods of manufacture are provided in Table 4. General production of a red algae extract includes harvesting, washing to remove epiphytes/sand, drying, grinding, addition of a solvent and preservative, filtration, quality control, and packaging.[5-7] Typical solvents include water, caprylic/capric triglycerides, and butylene glycol.

Composition and Impurities

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.[8] Red algae also contain proteins, polyphenols, polysaccharides, minerals, and amino acids. In addition, red algae may accumulate compounds like arsenic and antimony, and toxic metals such as cadmium, lead, mercury, tin, and aluminum.[9] The accumulation of these contaminants is influenced by environmental factors and structural features of the algae.

Ahnfeltiopsis Concinna Extract

A trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract was reported to have less than 20 ppm heavy metals and less than 2 ppm arsenic.[10]

Betaphycus Gelatinum Extract

A trade name mixture containing 1.5% Betaphycus Gelatinum Extract was reported to have less than 20 ppm heavy metals and not more than 2 ppm arsenic.[11]

Ceramium Kondoi Extract

A mixture containing 0.17% Ceramium Kondoi Extract and 0.83% saccharina angustata extract was reported to have less than 20 ppm heavy metals and not more than 5 ppm arsenic.[12]

Chondrus Crispus Extract

The composition of dried *Chondrus crispus* was reported to be 76.8% moisture, 27.7% ash, 4.58% potassium, 0.0736% iodine, 2.16% crude fiber, and 1.65% nitrogen.[13] Trade name mixtures containing Chondrus Crispus Extract (20% and 3.5%) were reported to have < 20 ppm heavy metals, < 10 ppm lead, < 2 ppm arsenic, and < 1 ppm cadmium.[14]

Corallina Officinalis Extract

A mixture of water and Corallina Officinalis Extract (0.2 – 4%) was reported to contain vitamin C (140 µg/100 ml), vitamin B1 (35 µg/100 ml), vitamin B2 (75 µg/100 ml), vitamin B3 (386 µg/100 ml), vitamin B6 (26 µg/100 ml) and vitamin PP (2.61 µg/100 ml).[15] This mixture also contains chlorides (2500 mg/l), nitrogen (431 mg/l), calcium (50 - 250 mg/l), magnesium (50 – 250 mg/l), phosphorus (17 mg/l), zinc (6.2 mg/l), iron (2.1 mg/l), potassium (1.1 mg/l), and iodine (< 9 mg/kg). The amount of iodine in a mixture of Corallina Officinalis Extract (0.2 – 4% algae), propylene glycol, and calcium chloride was determined to be < 1 mg/kg via a colorimetry assay.[15] A mixture containing Corallina Officinalis Extract (0.2 – 4% algae), calcium carbonate, sea water, and calcium chloride, was reported to contain 10 – 25 g/l magnesium.

A mineral and heavy metal analysis was performed on a trade name mixture consisting of 50% glycerin, 30% water, 18.5% undaria pinnatifida extract (a brown algae), and 1.5% Corallina Officinalis Extract; Table 5.[16] Iodine, arsenic, cadmium, mercury, and lead were present in amounts of 1.9 mg/l, 1383 µg/kg, 29 µg/kg, < 10 µg/kg, and 86 µg/kg, respectively.

Cyanidium Caldarium Extract

The major lipids in algae samples of *Cyanidium caldarium* include monogalactosyl diglyceride, digalactosyl diglyceride, plant sulfolipid, lecithin, phosphatidyl glycerol, phosphatidyl inositol, and phosphatidyl ethanolamine.[17] The fatty acid composition is variable, but major fatty acids include palmitic acid, oleic acid, linoleic acid, and stearic acid.

Delesseria Sanguinea Extract

The chemical composition of *Delesseria sanguinea* is characterized by two non-halogenated phenolic compounds of original structure: cyclohexadienone and delesserin.[18] Sterols such as cholesterol, 22-dehydrocholesterol, 7-dehydrocholesterol, and nor-24-cholestadiene-5, 22-ol-3β may be found in this species. A mixture consisting of Delesseria Sanguinea Extract (0.2 – 4% algae), water, and dipropylene glycol was reported to contain < 9 ppm iodine, 0.064 ppm arsenic, 0.168 ppm chromium, and no antimony, nickel, cobalt, silver, cadmium, lead, or mercury.

Digenea Simplex Extract

A *Digenea simplex* sample was reported to contain sodium, calcium, phosphorus, magnesium, potassium, and lead, in amounts of 1198, 432, 368, 398, 7744, and 0.01 mg/100 g dry weight, respectively.[19] The most prevalent fatty acids found in this sample were palmitic (14.02 mg/g), arachidic (30.78 mg/g), palmitoleic (6.50 mg/g), and linoleic (6.52 mg/g) fatty acids. Non-essential and essential amino acids were present in amounts of 28.52 and 40.78 g/100 g, respectively. Amino acids present in the largest quantities included aspartic acid (5.01 g/100 g), glutamic acid (7.50 g/100 g), tyrosine (4.40 g/100 g), leucine (5.70 g/100 g), lysine (6.50 g/100 g), methionine (4.87 g/100 g), phenylalanine (10.74 g/100 g), and threonine (7.52 g/100 g). In addition, kainic acid has been reported to be present in *Digenea simplex*.[20]

Furcellaria Lumbricalis Extract

A mixture of Furcellaria Lumbricalis Extract (0.2 – 4% algae), water, and sea salt, was reported to contain 1.6 – 2.4 g/l galactose.[21] The amount of arsenic, cadmium, mercury, and lead in this mixture were below 0.025 mg/kg. In addition, the mixture contained <1 mg/kg iodine, and < 0.125 mg/kg nickel, chromium, cobalt, silver, and antimony.

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).[22] 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.[23]

Gelidium Sesquipedale Extract

A heavy metal and mineral analysis was performed on a trade name mixture containing 4% Gelidium Sesquipedale Extract; Table 6.[24] Iodine was detected in an amount of 1.02 mg/kg, respectively. All other evaluated minerals and metals were present at 98.3 mg/100g or less.

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 (GC/MS).[25] 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 7.

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.[26] 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%) (percentages are in terms of the total amount of MAAs).

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.[27] 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 GC/MS.[28] 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.[29] According to a supplier, Hypnea Musciformis Extract is reported to be composed of 75% sugars (mainly polysaccharides which average molecular weight is below 700 kDa), 22% mineral ashes, and 3% proteins.[30] A heavy metal analysis performed on a Hypnea Musciformis Extract detected the following impurities: 0.082 ppm arsenic, < 0.020 ppm cadmium, < 0.020 ppm cobalt, 0.052 ppm chromium, < 0.020 ppm mercury, 0.185 ppm nickel, < 0.020 ppm lead, < 0.020 ppm antimony, 0.031 ppm selenium, and 0.053 ppm vanadium.[30] In addition, the sum of aflatoxins B1, B2, G1, and G2 in the Hypnea Musciformis Extract did not exceed 0.4 µg/kg.

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.[31]

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.[20] 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*. 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.[32] According to a manufacturer, Palmaria Palmata Extract is reported to be composed of 73% sugars (mainly oligosaccharides, average molecular weight between 540 and 2000 Da), 24% mineral ashes, and 3% proteins.[30]

Levels of iodine in *Palmaria palmata* can exhibit a wide range of value (10 - 100 µg/g) depending on location and time of harvest.[20] 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.[33] 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.

According to a heavy metal analysis performed by a supplier, antimony, arsenic, chromium, nickel, and vanadium, were detected in a Palmaria Palmata Extract in amounts of 0.069, 1.480, 0.046, 0.433, and 2.29 ppm, respectively.[30] Approximately 3.8 ppm iodine was detected in the same extract. No aflatoxins were detected in this Palmaria Palmata Extract.

Porphyra Umbilicalis Extract

The heavy metal impurities of trade name mixture containing Porphyra Umbilicalis Extract was reported to be < 3.0 ppm arsenic, < 0.1 ppm cadmium, < 1.0 ppm lead, < 0.1 ppm mercury, < 0.5 ppm antimony, < 1.0 ppm chromium, < 1.0 ppm nickel, and < 0.5 ppm cobalt.[34] Due to manufacturing processes, traces of residual phenol (< 0.1 ppm) and ethylene oxide (< 0.02 ppm) may be present in this Porphyra Umbilicalis Extract. Heavy metals detected in a different Porphyra Umbilicalis Extract include 3679 µg/kg arsenic, < 10 µg/kg cadmium, < 10 µg/kg mercury, and < 10 µg/kg lead.[35]

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.[36] 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).

Dried nori (*Porphyra* sp.) samples contained none or trace amounts of inorganic arsenic and total arsenic content.[36] 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 amounts varying from 0.58 – 11 mg/kg of DW.

Porphyra Tenera Extract, Porphyra Umbilicalis Extract, Porphyra Yezoensis Extract, Chondrus Crispus, Palmaria Palmata Extract, Gelidium Amansii Extract, Gelidium Cartilagineum Extract, Gelidium Sesquipedale, Lithothamnion Calcareum Extract and Gracilaria Verrucosa Extract

Heavy metal and metalloid contents in several edible red algae species (*Porphyra* sp., *Chondrus crispus*, *Palmaria Palmata*, *Gracilaria* sp.) based on geographical location evaluated.[37] Aluminum was present in *Gracilaria* species from Italy, *Palmaria palmata* from Spain, and *Porphyra* species from Spain in amounts of 19-149 mg/kg, 62 mg/kg DW, and 15-890 mg/kg DW, respectively. The concentration levels of 20 metals were analyzed by inductively coupled plasma atomic emission spectroscopy in various dehydrated red seaweed genera (*Chondrus, Gelidium, Palmaria, Porphyra,* and *Gracilaria*), from two origins (Asia and Europe).[38] The mean metal content in seaweed samples for the different genera of red algae is presented in Table 8. 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.

Palmaria palmata, *Porphyra umbilicalis*, *Porphyra tenera*, *Porphyra yezoensis*, *Chondrus crispus*, *Gracilaria verrucosa*, and *Lithothamnion calcareum* are authorized as vegetables and condiments in France, with certain specifications.[9] Maximum allowed 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).

Gigartina Stellata Extract, Corallina Officinalis Extract, and Kappaphycus Alvarezii Extract

A mineral and heavy metal analysis was performed on a trade name mixture containing water (45.7%), glycerin (40%), *Gigartina stellata* (4.43%), Kappaphycus Alvarezii Extract (5.9%), and Corallina Officinalis Extract; Table 9.[39] Sodium, chlorides, and potassium were detected at levels of 419.9 mg/100 g, 391 mg/100 g, and 109.4 mg/100 g, respectively. All other minerals and metals were detected in an amount of 11.9 mg/100 g or less.

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.

Collectively, based on VCRP and Council survey data, 26 of the red algae-derived ingredients are reported to be in use. According to 2021 VCRP survey data, Chondrus Crispus Extract is reported to be used in 268 formulations (222 leave-on formulations, 45 rinse-off formulations, and 1 formulation diluted for bath; Table 10).[40] Chondrus Crispus is reported to be used in 94 formulations, Corallina Officinalis Extract is reported to be used in 66 formulations, and Chondrus Crispus Powder is reported

to be used in 63 formulations. All other in-use ingredients are reported to be used in 52 formulations or less. The results of the concentration of use survey conducted by Council in 2020 indicate Corallina Officinalis Extract has the highest reported maximum concentration of use; it is used at up to 2% in blushers, other makeup preparations, and face and neck products.[41]

In some cases, reports of uses were received in the VCRP, but concentration of use data were not provided. For example, Ahnfeltiopsis Concinna Extract is reported to be used in 16 formulations, but no concentration of use data were reported. In other cases, no uses were reported in the VCRP, but concentration of use data were reported in the industry survey; e.g., Rhodymenia Palmata Extract had no reported uses in the VCRP, but a use concentration in eye lotions and face and neck products was provided in the industry survey. Therefore, it should be presumed there is at least one use in every category for which a concentration is reported. The 34 ingredients not in use, according to the VCRP and concentration of use survey data, are listed in Table 11.

Several of these ingredients are used in formulations that are used near the eye. For example, Chondrus Crispus Extract is reported to be used in eyeshadows at up to 0.14%. Incidental ingestion and/or contact with mucous membranes may also occur (e.g., Chondrus Crispus is reported to be used at up to 1.4% in dentifrices).

Additionally, some red algae-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Chondrus Crispus is reported to be used at up to 0.08% in aerosol suntan products. 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.[42,43] 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.[44,45] Red-algae derived ingredients have also been reported to be used in face powders that could possibly be inhaled (e.g., Chondrus Crispus Extract is reported to be used in face powders at up to 0.15%). 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 workplace.[46-48]

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.[49]

Non-Cosmetic

Several species of red algae (e.g., *Palmaria palmata*) have become established as part of popular international cuisine.[50] 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).[51] Due to its high mineral content, *Corallina officinalis* can be used as an emulsifier in the food industry in several products such as soft drinks, cakes, and candies.[52] A listing of red algae species that are frequently ingested by humans as foods is provided in Table 12.

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.[51] *Gloiopeltis tenax* has also been reported to be used in China to treat diarrhea and colitis.[25] In Japan and the Mediterranean area, *Gelidium cartilagineum* and *Chondrus Crispus* were used in diarrhea and urinary tract irritation treatment.[51] 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.[53] 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.[54] 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.[27] *Grateloupia livida* is also an edible and medicinal seaweed used to treat sore throat, stomachache, ascariasis, and dysentery.[55] 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.[29,51] *Corallina officinalis* extract is a popular ingredient in traditional Asian medicine used for the treatment of various ailments.[56] Several red algae species (e.g. *Chondrus crispus* (Irish moss) and *Gelidiella acerosa*) are widely used for the preparation of carrageenan, agar and for other industrial uses.[22,57]

TOXICOKINETIC STUDIES

No toxicokinetic studies on these ingredients were found in the published literature, and unpublished data were not submitted. In general, toxicokinetics data are not expected to be found on algal ingredients because each natural sourced ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Animal

Oral

Asparagopsis Armata Extract

An acute oral toxicity assay was performed according to Organisation for Economic Co-operation and Development Test Guidelines (OECD TG) 423.[58] The test substance (100% dry extract Asparagopsis Armata Extract; up to 2000 mg/kg) was administered to rats (strain not reported) via an oral route (method of oral administration and dose not stated). No other details regarding this study were provided. The median lethal dose (LD_{50}) was reported to be > 2000 mg/kg.

Corallina Officinalis Extract

The acute oral toxicity of a mixture containing water and Corallina Officinalis Extract (0.2 – 4% algae) was evaluated in 10 rats (strain not reported).[15] Animals (number of animals not reported) received the test substance, undiluted, via ingestion. The LD_{50} was reported to be > 5000 mg/kg. No other details regarding this study were provided.

Delesseria Sanguinea Extract

Acute oral toxicity of a mixture consisting of Delesseria Sanguinea Extract (0.2 – 4 % algae), water, and dipropylene glycol, was evaluated in 10 rats (strain not reported).[18] The test substance was given undiluted. The method of oral administration was not stated. The LD_{50} was reported to be > 2000 mg/kg.

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 Kumming mice (20/group).[28] 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 LD_{50} values were expected to be > 2000 mg/kg.

Lithothamnion Calcareum Extract

A *Lithothamnion calcareum* aqueous suspension was evaluated for acute oral toxicity in groups of 5 female Wistar rats.[54] 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, and 30 min, and each hour for 12 h. The rats were also examined twice a day for an additional 13 d. After 14 d, rats were euthanized and subjected to macroscopic and microscopic necropsy. No signs of toxicity were observed in any of the treated rats.

Short-Term Toxicity Studies

Human

Dermal

Corallina Officinalis Extract

A microcirculation assay was performed on 30 subjects using a mixture containing Corallina Officinalis Extract (0.2 – 4% algae) and water.[15] A 5% dilution of the mixture was placed on the skin for 27 consecutive days. The test substance was considered to be well-tolerated. No other details regarding this study was provided.

Subchronic Toxicity Studies

Animal

Oral

Lithothamnion Calcareum Extract

A *Lithothamnion calcareum* aqueous suspension was evaluated for oral toxicity in Wistar rats.[54] 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 (specific use of satellite groups not specified). A constant volume of *Lithothamnion calcareum* suspension (1000 or 2000 mg/kg) was administered to all test groups (including satellite groups), daily, via gavage, for 90 d. 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. Gross necropsy and histopathologic evaluation of 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.[59] 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 days 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. On day 8 of pregnancy, animals were laparotomized and evaluated. 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. At first laparotomy, 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. At second laparotomy, 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

Summaries of the in vitro genotoxicity studies summarized below are provided in Table 13.

Ames assays performed on an Asparagopsis Armata Extract (containing 8% dry algal matter; up to 5000 µg/plate), a mixture containing Asparagopsis Armata Extract (80%) and methylpropanediol (20%) (test concentration not reported), a mixture consisting of Corallina Officinalis Extract (0.2 – 4%) and water (test concentration not reported), a mixture containing Corallina Officinalis Extract (0.2 – 4% algae), sea water, calcium carbonate, and calcium chloride (test concentration not reported), a trade name mixture containing Corallina Officinalis Extract (3.97%), Kappaphycus Alvarezii Extract (5.9%), and *Gigartina stellata* (4.43%) (up to 5000 µg/plate), and a *Gelidiella acerosa* extract (up to 4000 µg/plate), yielded negative results.[15,58,60-62] A chemiluminescent 3D genotoxicity assay performed on a test substance containing 48% Porphyra Umbilicalis Extract also yielded negative results.[63]

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).[64] 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 wk. Rats in group 4 received 200 mg/kg bw *Hypnea musciformis* extract alone, each day, orally, for 16 wk. (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.[65] For the cell viability and proliferation studies, extracts (1000 µg/ml) were incubated with HepG-2 cells for 24 h. 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).[66] Tumors were induced in all experimental animals via a weekly subcutaneous injection of 1,2-dimethylhydrazine (DMH) for 12 wk. Experimental animals were fed a dietary seaweed preparation containing 2% *Porphyra tenera* powder, and controls were fed a basic diet. Animals were necropsied 8 wk 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).[67] Concentrations used were not reported. 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.

Gracilaria Verrucosa Extract

The potential cytotoxicity of a crude aqueous *Gracilariopsis longissima* extract (equivalent to *Gracilaria verrucosa* extract) was evaluated by a 3-(4,5-dimethylthiazol-2yl)-diphenyl tetrazolium bromide (MTT) assay.[26] 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 h. No cytotoxicity was observed in either human cell line (HGF or HaCaT) at any concentration; however, 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*.[68] Four groups of four hairless mice were treated with topical formulations on the dorsum for 5 d 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 ultraviolet A (UVA)/ultraviolet B (UVB) radiation for 28 min, 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 tumor antigen p53 and apoptosis mediator 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.[69] Control and treated groups were given a regular diet for 7 d. 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 h later, the thickness of the ear lobe was measured. Oral administration of porphyran at 2% significantly suppressed ear edema induced by TNCB. 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

The dermal irritation and sensitization studies summarized below are presented in Table 14.

In vitro dermal irritation assays were performed on a trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract (tested at 100%; other components of mixture not reported), an Asparagopsis Armata Extract containing 4% dry algal matter (tested at 10%; other components of extract not reported), a mixture containing 80% Asparagopsis Armata Extract and 20% methylpropanediol (tested at 100%), a trade name mixture containing 3.5% Chondrus Crispus Extract (tested at 100%; other component of mixture not reported), and a mixture consisting of Corallina Officinalis Extract (0.2 – 4% algae), propylene glycol, calcium chloride, and sea water (tested at 100%).[15,58,60,70,71] All test substances were predicted to be non-irritating.

No irritation was reported in animal dermal irritation assay in which rabbits (strain not reported) were dermally exposed to an undiluted mixture containing Corallina Officinalis Extract (0.2 – 4% algae) and water.[15] Similarly, no irritation was reported when a mixture consisting of Delesseria Sanguinea (0.2 – 4% algae), water, and dipropylene glycol, was applied to the skin of 3 rabbits (strain not reported).[18] The test concentration was not provided.

Many human dermal irritation studies were conducted using test substances containing a red algae-derived ingredient, or combination of ingredients, along with other substances such as water, propanediol, glycerin, and butylene glycol. The majority of these studies yielded negative results; however, slight irritation was noted (at 30 min after patch removal) in a 24-h patch test assay in which the undiluted test substance (trade name mixture consisting of 72 - 77% water; 20 - 70% butylene glycol; 1 - 3% Hypnea Musciformis Extract; ≤ 1% potassium gluconate; 0.16 - 0.2% methylparaben) was applied to the skin of 12 subjects under occlusive conditions.[72]

Numerous sensitization studies were performed using human subjects, and all results were negative. The following ingredients were evaluated: product containing 0.325% Asparagopsis Armata Extract; trade name mixture containing 0.3 – 2% Asparagopsis Armata Extract; mixture containing 7% Betaphycus Gelatinum Extract; product containing 0.49% Chondrus Crispus Extract; mixture containing 0.2 – 4% Corallina Officinalis Extract; formulation containing 2% Corallina Officinalis Extract; mixture containing 0.2 – 4% Delesseria Sanguinea Extract; mixtures containing 0.2 – 4% Furcellaria Lumbricalis Extract; product containing 0.0028% Gelidiella Acerosa Extract; trade name mixture containing < 2% Gelidium Cartilagineum Extract; mixture containing 0.5 – 3% Hydrolyzed Corallina Officinalis Extract; Hypnea Musciformis Extract (15%; 0.36% dry matter); trade name mixture containing 0.8% Kappaphycus Alvarezii Extract; Palmaria Palmata Extract (25%; 1.87% dry matter) in water; product containing 0.0004% Porphyra Umbilicalis Extract; and a formulation containing 0.000545% Porphyridium Cruentum Extract.[15,18,21,30,73-83]

Phototoxicity

In Vitro

Corallina Officinalis Extract

The potential phototoxicity of a mixture containing Corallina Officinalis Extract (0.2 – 4% algae) and water was evaluated in a 3T3 neutral red uptake (NRU) phototoxicity assay performed according to OECD TG 432.[15] Cytotoxicity was evaluated in a cell monolayer (fibroblast Balb/c3Tc clone) after incubation with the test substance at 7 concentrations (concentrations not specified), and irradiation with UVA. The test substance was considered to be non-cytotoxic. The same procedure was performed using a test substance consisting of Corallina Officinalis Extract (0.2 – 4% algae), sea water, calcium carbonate, and calcium chloride. No signs of phototoxicity were observed.

Porphyra Umbilicalis Extract

The phototoxic potential of a test substance consisting of 52% water and 48% Porphyra Umbilicalis Extract was evaluated according to the same procedure as above.[63] The test substance was considered to be non-cytotoxic.

OCULAR IRRITATION STUDIES

The ocular irritation studies summarized below are presented in Table 15.

In Vitro

An in vitro ocular irritation assay performed on reconstructed cornea epithelium using a trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract yielded negative results.[70] MatTek EpiOcular™ MTT viability assays were performed to evaluate the ocular irritation potential of three different test substances containing red algae-derived ingredients (an after-shave balm containing 0.8% Chondrus Crispus, a trade name mixture containing 3.5% Chondrus Crispus Extract, or an eye cream containing 0.0375% Rhodymenia Palmata Extract).[71,84,85] All test substances were considered to be non-irritating.

Slight irritation was noted in an in vitro ocular irritation assay performed using the PREDISAFE method on an Asparagopsis Armata Extract (4% dry algal matter).[60] According to summary data, a mixture containing Corallina Officinalis Extract (0.2 – 4% algae) sea water, calcium chloride, and propylene glycol was slightly irritating in a PREDISAFE assay.[15] A mixture containing Delesseria Sanguinea Extract (0.2 – 4% algae), water, and dipropylene glycol, was not considered to be a ocular irritant in a neutral red release assay.[18] No other details regarding this study were provided.

Several hen's egg test chorioallantoic membrane (HET-CAM) assays were performed on various red algae-derived ingredients (Asparagopsis Armata Extract (98.6%), Corallina Officinalis Extract (0.15%, 0.397%), Kappaphycus Alvarezii Extract (5.9%), Lithothamnion Calcareum Powder (up to 5.7 – 6.1%), and Porphyra Umbilicalis Extract (48%)). Most assays reported slight or no irritation.[58,63,85-88] However, moderate irritation was noted when a trade name mixture consisting of 57 - 61% Lithothamnion Calcareum Powder, 26 - 31% mannitol, 9 - 11% diatomaceous earth, 0.7 - 1.5% zinc sulfate was used in a HET-CAM assay tested at 10%, but not at 2 and 5%.

An agar diffusion cytotoxicity assay was performed in order to determine the ocular irritation potential of a mixture consisting of Furcellaria Lumbricalis Extract (0.2 – 4%), water, and sea salt.[21] Cytotoxicity was reported to be low, supporting a lack of ocular irritation. No other details regarding this study were provided.

Animal

According to summary data, Corallina Officinalis Extract (0.2 – 4% algae) in water was slightly irritating when applied undiluted to the eyes of 3 rabbits (strain not reported).[15] Similarly, slight irritation was observed in an ocular irritation study in which Delesseria Sanguinea Extract (0.2 – 4% algae) in dipropylene glycol and water was applied to the eyes of three rabbits (strain not reported). Details regarding these studies were not reported.[18]

SUMMARY

This is a safety assessment of 60 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 2021 VCRP survey data, Chondrus Crispus Extract is reported to be used in 268 formulations (222 leave-on formulations, 45 rinse-off formulations, and 1 formulation diluted for bath). Chondrus Crispus is reported to be used in 94 formulations, Corallina Officinalis Extract is reported to be used in 66 formulations, and Chondrus Crispus Powder is reported to be used in 63 formulations. All other in-use ingredients are reported to be used in 52 formulations or less. The results of the 2020 concentration of use survey conducted by Council indicate that Corallina Officinalis Extract has the highest reported maximum concentration of use; it is used at up to 2% in leave-on dermal products. All other in-use ingredients are reported to be used at 1.4% or less.

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.

No toxicity was observed in an acute oral toxicity study involving rats given up to 2000 mg/kg of an undiluted dry Asparagopsis Armata Extract. The oral LD_{50} was reported to be > 5000 mg/kg in an acute toxicity assay using a mixture containing Corallina Officinalis Extract (0.2 – 4% algae) in rats. In an acute oral toxicity assay performed on rats, using a test substance containing Delesseria Sanguinea Extract (0.2 – 4% algae), the LD_{50} was reported to be > 2000 mg/kg. 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.

A 27-d microcirculation assay was performed on 30 subjects. The test substance (Corallina Officinalis Extract (0.2 – 4% algae in water) was considered to be well-tolerated. A 90-d oral toxicity study was performed in which Wistar rats were given either 1000 or 2000 mg/kg/d of a Lithothamnion Calcareum 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 days 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 first laparotomized on day 8 of gestation, and allowed to recover. Animals were then re-laparotomized and evaluated on day 14 of gestation. At first laparotomy, 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 ($p < 0.001$).

Ames assays performed on an Asparagopsis Armata Extract (containing 8% dry algal matter), a mixture containing Asparagopsis Armata Extract (80%) and methylpropanediol (20%), a mixture consisting of Corallina Officinalis Extract (0.2 – 4%) and water, a mixture containing Corallina Officinalis Extract (0.2 – 4% algae), sea water, calcium carbonate, and calcium chloride, a trade name mixture containing Corallina Officinalis Extract (3.97%), Kappaphycus Alvarezii Extract (5.9%), and *Gigartina stellata* (4.43%), and a *Gelidiella acerosa* extract, yielded negative results. A chemiluminescent 3D genotoxicity assay performed on a test substance containing 48% Porphyra Umbilicalis Extract also yielded negative results.

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, for 16 wk. 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 *Asparagopsis 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. 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 wk, 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.[67] 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 h. 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 UV radiation. 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. Induced ear edema was evaluated after treatment with porphyran in the diet at up to 2%, for 7 d. Oral administration of porphyran at 2% significantly suppressed ear edema induced by TNCB. 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.

In vitro dermal irritation assays were performed on trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract (tested at 100%; other components of mixture not reported), an Asparagopsis Armata Extract containing 4% dry algal matter (tested at 10%; other components of extract not reported), a mixture containing 80% Asparagopsis Armata Extract and 20% methylpropanediol (tested at 100%), a trade name mixture containing 3.5% Chondrus Crispus Extract (tested at 100%; other component of mixture not reported), and a mixture consisting of Corallina Officinalis Extract (0.2 – 4%), propylene glycol, calcium chloride, and sea water (tested at 100%). All test substances were considered to be non-irritating.

No irritation was reported in animal dermal irritation assays in which rabbits were dermally exposed to a mixture containing Corallina Officinalis Extract (0.2 – 4% algae) and water (tested at 100%), or a mixture containing Delesseria Sanguinea Extract (0.2 – 4%), water, and dipropylene glycol (test concentration not reported). Many human dermal irritation studies were conducted using test substances containing a red algae ingredient, or combination of ingredients, along with other substances such as water, propanediol, glycerin, and butylene glycol. The majority of these studies yielded negative results; however, slight irritation was noted (at 30 min after patch removal) in a 24-h patch test assay on a trade name mixture containing 72 - 77% water; 20 - 70% butylene glycol; 1 - 3% Hypnea Musciformis Extract; ≤ 1% potassium gluconate; 0.16 - 0.2% methylparaben. All sensitization studies performed on humans, evaluating various red algae-derived ingredients (Asparagopsis Armata Extract (0.325% and 0.5 – 2%), Betaphycus Gelatinum Extract (7%), Chondrus Crispus Extract (0.49%), Corallina Officinalis Extract (0.2 – 4% algae), Corallina Officinalis Extract (2%), Delesseria Sanguinea Extract (0.2 – 4% algae), Furcellaria Lumbricalis Extract (0.2 – 4% algae), Gelidiella Acerosa Extract (0.0028%), Gelidium Cartilagineum Extract (< 2%), Hydrolyzed Corallina Officinalis Extract (0.5 – 3%), Hypnea Musciformis Extract (15% (0.36% dry matter)), Kappaphycus Alvarezii Extract (0.8%), Palmaria Palmata

Extract (25% (1.87% dry matter)), Porphyra Umbilicalis Extract (0.0004%), and Porphyridium Cruentum Extract (0.000545%)) were negative.

3T3 NRU phototoxicity assays were performed on two different mixtures containing Corallina Officinalis Extract (0.2 – 4% algae), and a mixture of Porphyra Umbilicalis Extract (48%) and water. These test substances were considered to be non-cytotoxic.

No irritation was observed in in vitro ocular assays performed on a trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract, a mixture containing 98.6% Asparagopsis Armata Extract, an after-shave balm containing 0.8% Chondrus Crispus, a trade name mixture containing 3.5% Chondrus Crispus Extract, a trade name mixture containing 1.5% Corallina Officinalis Extract, a mixture containing 0.2 – 4% Delesseria Sanguinea Extract, and a mixture containing 0.2 – 4% Furcellaria Lumbricalis Extract. Slight irritation was observed in a PREDISAFE assay evaluating an Asparagopsis Armata Extract (4% dry algal matter). Slight irritation was also observed in a HET-CAM assay using a test substance containing *Gigartina stellata* (4.43%), Kappaphycus Alvarezii Extract (5.9%), and Corallina Officinalis Extract (3.97%). Moderate irritation was noted when a trade name mixture containing 57 - 61% Lithothamnion Calcareum Powder was used in a HET-CAM assay and tested at 10%, but not when tested at 2 and 5%. In vivo Ocular irritation assays performed in rabbits revealed slight irritation when exposed to Corallina Officinalis Extract (0.2 – 4% algae) in water and Delesseria Sanguinea Extract (0.2 – 4% algae) in water and dipropylene glycol.

DISCUSSION

The Panel reviewed the red algae-derived ingredients in this report, and concluded that although 16 of the 60 ingredients are safe as used in cosmetics in the present practices of use, data were insufficient to determine the safety of the remaining 44 ingredients. Ingredient data profiles were considered sufficient when composition data or systemic toxicity data (via use in food, GRAS designation for food use, or oral toxicity) and sensitization data were available. (The need for systemic toxicity data was mitigated for those ingredients that are used in foods or are considered GRAS, because exposure via ingestion would be far greater than exposure via cosmetics.) Ingredients lacking some or all of these data components were considered to have insufficient safety data, and depending on which data were lacking, systemic toxicity data, sensitization data, or both are required. As for those ingredients that are formulated differently, but are derived from the same genus and species and would be similar in composition (e.g., Chondrus Crispus Extract and Chondrus Crispus Powder), the Panel confirmed that if there are sufficient data to support the safety of one of these ingredients, all related ingredients of the same genus and species would be considered safe as well.

The Panel noted that elevated levels of heavy metals, arsenic, and pesticide residues may be present in these red algae-derived ingredients. The Panel stressed that the cosmetics industry should continue to use cGMPs to limit these impurities. The Panel also noted the presence of kainic acid (a potential neurotoxin) and arachidonic acid (which was previously found by the Panel to have insufficient data to determine safety) in several of these red algae ingredients, and determined that concern for the presence of these constituents is mitigated as the final concentration of these substances would be minimal in cosmetic formulations.

The Panel discussed the issue of incidental inhalation exposure that could result with the use of some of these ingredients (e.g., up to 0.08% Chondrus Crispus in aerosol suntan products and 0.15% Chondrus Crispus Extract in face powders). Inhalation toxicity data were not available. However, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 16 of the 60 red algae-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

Chondrus Crispus
Chondrus Crispus Extract
Chondrus Crispus Powder
Corallina Officinalis Extract
Corallina Officinalis Powder*
Corallina Officinalis Thallus Extract*
Hydrolyzed Corallina Officinalis *
Hydrolyzed Corallina Officinalis Extract
Gelidiella Acerosa Extract
Hydrolyzed Chondrus Crispus Extract
Hypnea Musciformis Extract
Palmaria Palmata Extract
Palmaria Palmata Powder*
Porphyra Umbilicalis Extract
Porphyra Umbilicalis Powder*
Rhodymenia Palmata Extract

**Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.*

The Panel also concluded that the available data are insufficient to make a determination that the remaining 44 ingredients are safe under the intended conditions of use in cosmetic formulations.

Ahnfeltiopsis Concinna Extract
Asparagopsis Armata Extract
Betaphycus Gelatinum Extract**
Botryocladia Occidentalis Extract**
Calliblepharis Ciliata Extract**
Ceramium Kondoi Extract**
Ceramium Rubrum Extract**
Chondracanthus Teedei Powder**
Cyanidium Caldarium Extract
Delesseria Sanguinea Extract
Digenea Simplex Extract**
Dilsea Carnosa Extract**
Furcellaria Lumbricalis 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**
Hydrolyzed Porphyra Yezoensis**
Kappaphycus Alvarezii Extract
Lithothamnion Calcareum Extract
Lithothamnion Calcareum Powder
Lithothamnion Corallioides Powder**
Mesophyllum Lichenoides Extract**
Phymatolithon Calcareum Extract
Pikea Robusta Extract**
Polysiphonia Lanosa Extract**
Porphyra Linearis Powder**
Porphyra Tenera Extract**
Porphyra Tenera Sporophyte Extract**
Porphyra Yezoensis Extract
Porphyra Yezoensis Powder**
Porphyridium Cruentum Culture Conditioned Media**
Porphyridium Cruentum Extract
Porphyridium Purpureum Extract
Sarcodiotheca Gaudichaudii Extract**

*** There are currently no uses reported for these ingredients,*

Ingredients in blue type were considered sufficient in systemic toxicity data, however, sensitization data or composition data are required by the Panel to determine safety.
Ingredients in green type were considered sufficient in sensitization data, however, systemic toxicity data are required by the Panel to determine safety.
Ingredients in red type were considered insufficient in both systemic toxicity and sensitization data.

TABLES

Table 1. 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 ciliata.*	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
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

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

Ingredient	Definition	Function
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
Kappaphycus Alvarezii Extract	Kappaphycus Alvarezii Extract is the extract of the alga, *Kappaphycus alvarezii*	Skin-Conditioning Agents – Emollient; Skin-Conditioning Agents – Miscellaneous
Lithothamnion Calcareum Extract	*See Phymatolithon Calcareum Extract*	
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 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	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
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
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
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
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 2. Taxonomy of red-algae derived ingredients based on currently accepted scientific name[89]

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	Gigartinales	Solieriaceae	Kappaphycus	Kappaphycus Alvarezii 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
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 3. 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	[89,90]
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	-widely distributed in South and West -larger lower intertidal pools and subtidal on stones, maerl, and shells -occasionally abundant on bedrock	[89]
Chondrus crispus	-thallus of cartilaginous consistency, perennial, erect, expanding gradually onto a flat, fan-like or curled -variable in form -blade is dichotomously branched in tufts from a discoid holdfast -color of fronds vary depending on time of year and depth of water (white to yellowing green in the summer and in shallow water; dark purplish-red in autumn and deeper water)	-mainly distributed on Atlantic coasts of Europe, East Africa, and North America -found in lower intertidal and shallow subtidal stages -on rocks and stones and also in tide pools	[91]
Corallina officinalis	-calcified or calcareous red marine algae reaching 5-12 cm in height -erect articulated thallus arising from a firmly attached crustose base up to 70 mm in diameter and bearing tufts of branches and articulated fronds up to 120 mm long -varied in color; thallus appears to be dull purple when growing in deep water, becoming red yellow and finally white on exposure	-widely distributed in temperate areas on rocks, mid tidal pools and drainage runnels	[56]
Cyanidium caldarium	-unicellular -prefers low pH and high temperature for growth -contains phycocyanin	-mostly found in acidic hot springs and soils -reported to be found in the US, Italy, New Zealand, Japan, Iceland, and Central America -fresh water	[92]
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	[89]
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	[89]
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	[89]
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	[89]
Gelidium sesquipedale	-composed of several erect axes, compressed and branched -axes bear secondary aces with ramuli short and pinnate -the thallus appears robust with a cartilaginous consistency, dark red in color -can reach up to 25-30 cm long	-develops on rocks in semi-exposed to exposed locations in the lower intertidal and shallow subtidal level	[93]

Table 3. General characteristics and geographic distribution of several red algae species

Species	Description	Distribution/Habitat/Ecology	References
Gigartina stellata	-thallus bears dichotomously branches blades which arise form a basal discoid crust -stiff and cartilaginous -purplish-brown in color -10-20 cm high -stipe is narrow and compressed, expanding into strap-like blade, usually inrolled to form a channel	-found in large continuous mats on rocks, on exposed and semi-exposed sites in the low intertidal zone with some extension into the upper sublittoral	[94]
Kappaphycus alvarezii	-thallus shows a simple discoid hold-fast from which arises a main axis with irregular branches -morphology changes with habitat; thalli range from terete to foiliose -thalli can reach up to 2 m tall; their color is green or yellow	-origin is from Malaysia; the species occurs naturally in the Sulu Sea and the Sulu Archipelago -it has been naturalized in several western and central Pacific localities for farming purposes	[95]
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	[89]
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	[89]
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	[89]
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	[89]
Porphyra umbilicalis	-blades appear reddish brown, brownish, grey brown, or olive green in the field; in a dried state they are very thin and violet in color -blades constituted by a single cell layer can reach 60 cm in height	-common and abundant everywhere on the rocky parts of coasts or on beach pebbles on the Atlantic coasts of Europe (from Scandinavia to Morocco) and North America -appears in the upper littoral zone singly or in dense colonies	[96]
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	[89]

Table 4. Methods of manufacture for red algae-derived ingredients

Ingredient (characterization)	Method of Manufacture	Reference
Asparagopsis armata extract	fresh seaweed → wash → freeze → grind → extraction with 1:4 biomass:solvent ratio with methanol and dichloromethane	[97]
Asparagopsis Armata Extract	algae → grinding → extraction with water → stabilization with vegetable glycerin →filtration	[98]
Asparagopsis Armata Extract	fresh seaweed → grinding → cold cellular extraction → filtration → concentration → freeze-drying under neutral atmosphere	[99]
Asparagopsis Armata Extract	harvesting/identification → washing → grinding → extraction with solvents (propanediol and water) → filtration → quality control → packaging → quality control	[100]
Chondrus Crispus Extract and Gigartina Stellata Extract	harvesting/identification → washing → condensation of cellular water by soft drying → filtration and UV treatment → quality control → addition of preservatives and pH adjustment → quality control → packaging → quality control	[101]
Chondrus Crispus Powder	harvesting → naturally dried via sun exposure → grinding/sieving → packaging → sterilized via gamma ray treatment	[102]
Chondrus Crispus Powder	harvesting/identification → drying → cutting → ionization → quality control → packaging → quality control	[103]
Corallina Officinalis Extract, Gigartina Stellata Extract, and Kappaphycus Alvarezii Extract	dried grounded algae → extraction with water → testing → sifting → centrifugation → ultrafiltration → testing → homogenization → testing → sterile filtration → testing → packing	[104]
Corallina Officinalis Extract	dried grounded algae → extraction with water → testing → sifting → centrifugation → ultrafiltration → testing → homogenization → testing → sterile filtration → testing → packing	[105]
Digenea simplex extract	Dried algal powder (200 mg) extracted with 6 ml 80% methanol → ultrasonic bath → vortex → centrifuge → filtration → drying	[106]

Table 4. Methods of manufacture for red algae-derived ingredients

Ingredient (characterization)	Method of Manufacture	Reference
Gelidiella acerosa extract	100 g seaweed packed in Soxhlet apparatus → addition of solvent (petroleum ether, hexane, benzene, dichloromethane, chloroform, ethyl acetate, acetone, methanol, or water) → re-distillation → filtration→ placed in desiccator	62
Gelidium amansii extract	algae collection → washing → dried at room temperature → grinding → powder extracted with 80% ethanol for 24 h → freeze-drying	23
Gelidium Cartilagineum Extract	harvesting/identification → drying → grinding → extraction with solvent (caprylic/capric triglyceride) → addition of sterol → filtration → quality control → packaging → quality control	6
Gracilariopsis chorda extract	seaweed collection → mechanical washing → drying in room temperature → pulverization → extraction with 95% ethanol→ mixture placed in orbital shaker at 200 rpm → centrifugation → filtration → concentration → drying under steam of nitrogen gas	27
Hydrolyzed Corallina Officinalis Extract	harvesting/identification → extraction with water → addition of sodium methylparaben or 2-phenoxyethanol → filtration →quality control → packaging →quality control	5,107
Hypnea Musciformis Extract	harvesting/identification → drying → grinding → extraction with the solvent (water and butylene glycol) → addition of potassium gluconate and methylparaben → filtration →quality control → packaging → quality control	7
Hypnea Musciformis Extract	solubilization of *Hypnea musciformis* in water → separation of soluble and insoluble phases → filtration → membrane sterilization	30
Lithothamnion Calcareum Powder	harvesting → drying → grinding → micronisation → ionization → mixture → addition of mannitol, zinc sulfate, and diatomaceous earth → packaging → quality control	108
Palmaria Palmata Extract	solubilization of powder of *Palmaria palmata* in water → separation of soluble and insoluble phases → concentration of soluble phase → membrane sterilization	30
Porphyra Umbilicalis Extract	circular flow extraction of 7.8% dry algae on dry algae → in-process control → maturation at room temperature → filtration of the supernatant → cationic exchange → filtration → cross flow filtration → encapsulation of the extract into liposomes → packaging → quality control	34
Porphyra Umbilicalis Extract	dried grounded algae → extraction with water → testing → centrifugation → ultrafiltration → testing → sterile filtration → testing → packaging	109

Table 5. Mineral and metal analysis of a trade name mixture consisting of 50% glycerin; 30% water; 18.5 % undaria pinnatifida extract; and 1.5% Corallina officinalis Extract[16]

Determination	Results/Units
Sodium	420.4 mg/100 ml
Calcium	142.9 mg/100 ml
Phosphorus	8.9 mg/100 ml
Magnesium	60.7 mg/100 ml
Potassium	530.3 mg/100 ml
Copper	<0.5 mg/100 ml
Iron	<0.5 mg/100 ml
Manganese	0.0 mg/100 ml
Zinc	<0.5 mg/100 ml
Iodine	1.9 mg/l
Arsenic	1383 µg/kg
Cadmium	29 µg/kg
Mercury	<10 µg/kg
Lead	86 µg/kg
Selenium	<50 µg/kg
Silicon	0 mg/kg

Table 6. Mineral and metal analysis of a trade name mixture containing 4% Gelidium Sesquipedale Extract[24]

Analysis	Results ± Uncertainties	Units
Ashes	0.4 ± 0.2	g/100 g
Calcium	<4.0	mg/100 g
Magnesium	14.0 ± 1.4	mg/100 g
Phosphorus	<2.0	mg/100 g
Potassium	82 ± 8.2	mg/100 g
Sodium	98.3 ± 9.8	mg/100 g
Copper	<0.3	mg/100 g
Iron	<0.2	mg/100 g
Manganese	<0.3	mg/100 g
Zinc	<0.3	mg/100 g
Arsenic	72	µg/kg
Cadmium	<10	µg/kg
Mercury	<5	µg/kg
Molybdenum	<51	µg/kg
Lead	<10	µg/kg
Selenium	<811	µg/kg
Iodine	1.02	mg/kg

Table 7. Chemical composition of a supercritical carbon dioxide extract of *Gloiopeltis tenax*[25]

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
methyl 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 8. Mean metal content ± standard deviation in seaweed samples for different genera of red algae (mg/kg DW)[38]

	Chondrus (n = 2)	*Gelidium* (n = 2)	*Palmaria* (n = 4)	*Porphyra* (n = 10)	*Gracilaria (*n = 2*)*
Sodium	6799 ± 84.6	1279 ± 0	3803 ± 463	2274 ± 675	-
Arsenic	-	-	-	-	15
Potassium	9901 ± 270	543 ± 53.2	8044 ± 0	6563 ± 854	-
Calcium	2028 ± 153	908 ± 7.01	459 ± 0.00	1793 ± 1211	-
Cadmium	-	-	-	-	0.04 – 0.4
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	19 - 149
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	0.8 – 7

- = None reported

Table 9. Mineral and metal analysis of a trade name mixture containing water (45.7%), glycerin (40%), *Gigartina stellata* (4.43%), Kappaphycus Alvarezii Extract (5.9%), and Corallina Officinalis Extract (3.97%)[39]

Determination	**Results/Units**
Sodium	419.9 mg/100 g
Calcium	4.8 mg/100 g
Phosphorus	<2 mg/100 g
Chlorides	391 mg/100 g
Magnesium	11.9 mg/100 g
Potassium	109.4 mg/100 g
Copper	<0.5 mg/100 g
Iron	<0.5 mg/100 g
Manganese	<0.5 mg/100 g
Zinc	<0.5 mg/100 g
Iodine	1.2 mg/kg
Arsenic, inorganic	<0.15 mg/kg
Arsenic	116 µg/kg
Cadmium	<10 µg/kg
Mercury	<10 µg/kg
Lead	<10 µg/kg
Selenium	<10 µg/kg

Table 10. Frequency (2021) and concentration of use (2020) of red algae-derived ingredients[40,41,110]

	# 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*	**5**	**NR**	**18**	**0.031 – 0.33**	**94**	**0.00004 – 1.4**
Duration of Use						
Leave-On	*4*	*NR*	*16*	*0.031 – 0.33*	70	*0.00004 – 0.8*
Rinse-Off	*1*	*NR*	*2*	*0.1*	17	*0.005 – 1.4*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	7	*NR*
Exposure Type						
Eye Area	0	NR	8	0.031	12	0.12
Incidental Ingestion	NR	NR	NR	NR	5	1.4
Incidental Inhalation-Spray	2[a]; 1[b]	NR	4[a]; 3[b]	NR	18[a]; 27[b]	0.08; 0.005[b]
Incidental Inhalation-Powder	2[a]	NR	4[a]	0.063[c]	5; 18[a]	0.13; 0.51[c]
Dermal Contact	5	NR	18	0.031 – 0.063	86	0.08 - 0.8
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	0.1 – 0.33	3	0.00004 – 0.005
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	1	NR	20	0.3 – 1.4
Baby Products	NR	NR	NR	NR	NR	NR

	Chondrus Crispus Extract		Chondrus Crispus Powder		Corallina Officinalis Extract	
Totals*	**268**	**0.000003 – 0.5**	**63**	**0.1**	**66**	**0.00013 – 2**
Duration of Use						
Leave-On	*222*	*0.000003 – 0.49*	52	*0.1*	56	*0.000013 – 2*
Rinse Off	*45*	*0.0018 – 0.5*	11	*NR*	10	*0.00014 – 0.11*
Diluted for (Bath) Use	*1*	*NR*	NR	*NR*	NR	*NR*
Exposure Type						
Eye Area	37	0.14 – 0.3	12	0.1	2	0.0004 – 0.01
Incidental Ingestion	9	NR	6	NR	NR	NR
Incidental Inhalation-Spray	71[a]; 57[b]	0.001[b]	24[a]; 8[b]	NR	7[a]; 37[b]	NR
Incidental Inhalation-Powder	17; 71[a]	0.15; 0.0005 – 0.29[c]	24[a]	NR	1; 7[a]	2[c]
Dermal Contact	243	0.000003 – 0.5	56	0.1	61	0.00013 – 2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	14	0.001 – 0.0018	1	NR	1	NR
Hair-Coloring	NR	0.01	NR	NR	NR	NR
Nail	NR	NR	NR	NR	4	0.099
Mucous Membrane	13	NR	8	NR	NR	NR
Baby Products	NR	0.000003	NR	NR	NR	NR

	Cyanidium Caldarium Extract		Delesseria Sanguinea Extract		Furcellaria Lumbricalis Extract	
Totals*	**3**	**NR**	**2**	**NR**	**44**	**NR**
Duration of Use						
Leave-On	*3*	*NR*	*2*	*NR*	*44*	*NR*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	NR	3	NR
Incidental Ingestion	NR	NR	NR	NR	2	NR
Incidental Inhalation-Spray	3[b]	NR	1[a]; 1[b]	NR	10[a]; 16[b]	NR
Incidental Inhalation-Powder	NR	NR	1[a]	NR	10[a]	NR
Dermal Contact	3	NR	2	NR	42	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	2	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 10. Frequency (2021) and concentration of use (2020) of red algae-derived ingredients[40,41,110]

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Gelidium Amansii Extract		Gelidium Cartilagineum Extract		Gelidiella Acerosa Extract	
Totals*	**1**	**NR**	**36**	**NR**	**29**	**0.0001 – 0.028**
Duration of Use						
Leave-On	*1*	*NR*	*33*	*NR*	*14*	*0.00065 - 0.028*
Rinse-Off	*NR*	*NR*	*3*	*NR*	*15*	*0.0001 – 0.015*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	2	NR	3	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1[b]	NR	7[a]; 18[b]	NR	9[b]	NR
Incidental Inhalation-Powder	NR	NR	7[a]; 1[c]	NR	NR	0.007 – 0.028[c]
Dermal Contact	1	NR	36	NR	16	0.0001 – 0.028
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	9	0.0008
Hair-Coloring	NR	NR	NR	NR	4	0.0045
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	0.015
Baby Products	NR	NR	1	NR	NR	NR

	Gigartina Stellata Extract		Hydrolyzed Chondrus Crispus Extract		Hydrolyzed Corallina Officinalis Extract	
Totals*	**7**	**NR**	**1**	**0.012 – 0.017**	**4**	**NR**
Duration of Use						
Leave-On	*2*	*NR*	*1*	*0.012 – 0.017*	*4*	*NR*
Rinse-Off	*5*	*NR*	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	NR	0.012 – 0.017	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1[a]; 1[b]	NR	1[a]	NR	1[a]; 2[b]	NR
Incidental Inhalation-Powder	1[a]	NR	1[a]	NR	1[a]	NR
Dermal Contact	1	NR	1	0.012 – 0.017	4	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	6	NR	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Hypnea Musciformis Extract		Kappaphycus Alvarezii Extract		Lithothamnion Calcareum Extract	
Totals*	**52**	**0.0003 – 0.13**	**24**	**0.019 – 0.19**	**19**	**0.0059 – 0.037**
Duration of Use						
Leave-On	*18*	*0.0003 – 0.08*	*15*	*0.019 – 0.19*	*19*	*0.0059 – 0.037*
Rinse-Off	*34*	*0.0004 – 0.13*	*9*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	3	NR	1	NR	4	0.012
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1; 8[b]	0.03	8[a]; 4[b]	NR	1[a]; 2[b]	NR
Incidental Inhalation-Powder	NR	0.02 – 0.08[c]	8[a]	0.019 – 0.19[a]	1[a]	0.0059[c]
Dermal Contact	16	0.0003 – 0.13	16	0.019 – 0.19	1	0.0059 – 0.012
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	20	0.0045	8	NR	NR	NR
Hair-Coloring	15	NR	NR	NR	NR	NS
Nail	1	NR	NR	NR	12	0.037
Mucous Membrane	NR	0.13	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

Table 10. Frequency (2021) and concentration of use (2020) of red algae-derived ingredients[40,41,110]

	# 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*	**8**	**NR**	**52**	**0.0005 – 0.075**	**2**	**NR**
Duration of Use						
Leave-On	*3*	*NR*	*48*	*0.0005 – 0.075*	*2*	*NR*
Rinse-Off	*5*	*NR*	*4*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	3	NR	1	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	2[a]	NR	21[a]; 12[b]	0.0006	NR	NR
Incidental Inhalation-Powder	2[a]	NR	21[a]	0.075[c]	NR	NR
Dermal Contact	8	NR	50	0.0005 – 0.075	1	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	2	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	0.0005	1	NR
Mucous Membrane	NR	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Porphyra Umbilicalis Extract		Porphyra Yezoensis Extract		Porphyridium Cruentum Extract	
Totals*	**21**	**0.0004 – 0.0035**	**3**	**NR**	**35**	**0.00055 – 0.03**
Duration of Use						
Leave-On	*15*	*0.0004*	*3*	*NR*	*28*	*0.00055 – 0.03*
Rinse-Off	*5*	*0.0035*	*NR*	*NR*	*7*	*0.00055 – 0.017*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	NR	NR	1	*NR*	7	0.00055
Incidental Ingestion	NR	NR	NR	*NR*	NR	0.00055
Incidental Inhalation-Spray	7[a]; 7[b]	NR	1[a]; 1[b]	*NR*	7[a]; 9[b]	0.00055[b]
Incidental Inhalation-Powder	7[a]	NR	1[a]	*NR*	7[a]	0.03[c]
Dermal Contact	19	0.0004 – 0.0035	3	*NR*	35	0.00055 – 0.03
Deodorant (underarm)	NR	NR	NR	*NR*	NR	NR
Hair - Non-Coloring	2	NR	NR	*NR*	NR	0.00055
Hair-Coloring	NR	NR	NR	*NR*	NR	NR
Nail	NR	NR	NR	*NR*	NR	NR
Mucous Membrane	3	NR	NR	*NR*	NR	0.00055
Baby Products	NR	NR	NR	*NR*	NR	NR

	Porphyridium Purpureum Extract		Rhodymenia Palmata Extract	
Totals*	**5**	**NR**	**NR**	**0.038**
Duration of Use				
Leave-On	*5*	*NR*	*NR*	*0.038*
Rinse-Off	*NR*	*NR*	*NR*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*
Exposure Type				
Eye Area	NR	NR	NR	*0.038*
Incidental Ingestion	NR	NR	NR	NR
Incidental Inhalation-Spray	2[a]; 3[b]	NR	NR	NR
Incidental Inhalation-Powder	2[a]	NR	NR	0.038[c]
Dermal Contact	5	NR	NR	0.038
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR

*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

Table 11. Red algae-derived ingredients with no reported uses, according to the VCRP and Council survey

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

Table 12. 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	[111]
Chondrus crispus	Used as thickener/gelling agent; used in drinks; also known as Irish moss; eaten whole	[112]
Corallina officinalis	Emulsifying agent in food products	[52]
Gelidiella sp.	Used in jellies	[51]
Gelidium amansii	Used in jellies	[23]
Gigartina stellata	Used interchangeably with Chondrus crispus; thickener/gelling agent	[51,89]
Gracilaria sp.	Used in jellies	[51]
Gracilaria verrucosa	Eaten whole, with salads	[112]
Hypnea musciformis	Eaten whole, dried	[113]
Lithothamnion calcareum	Used as vegetables and condiments in France	[9]
Palmaria palmata	Eaten fresh or dry; used in breads and cakes	[30,50]
Porphyra tenera	Typically, dried and used to make sushi; nori, spices, seasoning, flavoring (GRAS)	21CFR184.1121, [36]
Porphyra umbilicalis	Typically, dried and used to make sushi	[96,112]
Porphyra yezoensis	Typically, dried and used to make sushi, nori	[36,114]
Rhodymenia palmata	Spices, seasoning, flavoring (GRAS)	21CFR184.1121

Table 13. **In Vitro Genotoxicity studies**

Ingredient	Test Substance	Concentration	Test System/Species/Conditions	Results	Reference
Asparagopsis Armata Extract	Asparagopsis Armata Extract (8% dry algal matter)	52, 164, 512, 1600, 5000 µg/plate	Ames test; *S. typhimurium* (strains TA98, TA100, TA1537, TA102); with and without metabolic activation	Negative	[60]
Asparagopsis Armata Extract	Mixture containing 80% Asparagopsis Armata Extract and 20% methylpropanediol	NR	Ames test; OECD TG 471; strains and use of metabolic activation not reported	Negative	[58]
Corallina Officinalis Extract	Corallina Officinalis Extract (0.2 – 4% algae) and water	NR	Ames test; OECD TG 471; performed using 4 strains of *S. typhimurium* and 1 strain of *E. coli* (strains not specified; with and without metabolic activation	Negative	[15]
Corallina Officinalis Extract	Corallina Officinalis Extract (0.2 – 4% algae), sea water, calcium carbonate, and calcium chloride	NR	Ames test; OECD TG 471; performed using 5 strains of *S. typhimurium* (strains not specified; with and without metabolic activation	Negative	[15]
Corallina Officinalis Extract, Gigartina Stellata Extract, and Kappaphycus Alvarezii Extract	Trade name mixture consisting of water (45.7%), glycerin (40%), *Gigartina stellata* (4.43%), Kappaphycus Alvarezii Extract (5.9%), and Corallina Officinalis Extract (3.97%)	50, 160, 500, 1600, 5000 µg/plate	Ames test; *S. typhimurium* (strains TA98, TA100, TA1535, TA1537, TA102); with and without metabolic activation	Negative	[61]
Gelidiella Acerosa Extract	Benzene extract of *Gelidiella acerosa*	250, 500, 1000, 2000, 4000 µg/plate	Ames test; *S. typhimurium* (strains TA98, TA100, TA1535); with and without metabolic activation	Negative	[62]
Porphyra Umbilicalis Extract	48% Porphyra Umbilicalis Extract and 52% water	2, 10, 25, 50, 100%	Chemiluminescent 3D assay; with and without UVB irradiation; positive control of chlorpromazine	Negative	[63]

Table 14. Dermal irritation and sensitization

Ingredient	Test Substance	Concentration/Dose of the test substance	Test Population/ # of test samples	Procedure	Results	Reference
IRRITATION						
In Vitro						
Ahnfeltiopsis Concinna Extract	Trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract (other components not reported)	100%; 30 µl (liquid) or 25 mg (solid)	3	Reconstructed human epidermal model; 3 tissues treated with test substance and incubated for 60 min	Non-irritating	[70]
Asparagopsis Armata Extract	An Asparagopsis Armata Extract containing 4% dry algal matter (other components not reported)	10%; 200 µl	2	Local tolerance evaluated in EPISKIN reconstructed human epidermis model; 18-h incubation	Non-irritating	[60]
Asparagopsis Armata Extract	A mixture containing 80% Asparagopsis Armata Extract (4 % dry algal matter) and 20% methylpropanediol	100%; dose not reported	NR	Reconstructed human epidermis model; OECD TG 439	Non-irritating	[58]
Chondrus Crispus Extract	Trade name mixture containing 3.5% Chondrus Crispus Extract (other components not reported)	100%; 20 µl	3	MatTek EpiDerm™ MTT Assay; 3 tissues treated	Non-irritating	[71]
Corallina Officinalis Extract	Mixture containing Corallina Officinalis (0.2 – 4% algae), sea water, calcium chloride, and propylene glycol	100%	NR	Reconstructed human epidermis model	Non-irritating	[15]
Animal						
Corallina Officinalis Extract	Mixture containing Corallina Officinalis Extract (0.2 – 4% algae) and water	100%; dose not reported	3 rabbits (strain not reported)	primary cutaneous tolerance assay	Non-irritating	[15]
Delesseria Sanguinea Extract	Mixture containing Delesseria Sanguinea Extract (0.2 – 4% algae), dipropylene glycol, and water	100%; dose not reported	3 rabbits (strain not reported)	primary cutaneous tolerance assay	Non-irritating	[18]
Human						
Asparagopsis Armata Extract	An Asparagopsis Armata Extract containing 4% dry algal matter in water	10%; 20 µl	10	48-h patch test under occlusive conditions	Non-irritating	[60]
Asparagopsis Armata Extract	Trade name mixture containing 0.5 –2% Asparagopsis Armata Extract, 56 – 62% water, and 38 – 42% propanediol	3%; 20 µl	22	48-h patch test under occlusive conditions	Non-irritating	[115]
Chondrus Crispus	After-shave balm containing 0.8% Chondrus Crispus	100%; 0.2 ml	30	23-h exposure per day for 14 d; occlusive conditions	Non-irritating	[116]
Chondrus Crispus Extract and Gigartina Stellata Extract	Trade name mixture containing Chondrus Crispus Extract and Gigartina Stellata Extract (98.10 – 98.95% extract, 0.80 – 1.10% sodium benzoate; 0.25 – 0.35% potassium sorbate; 0 -0.30% lactic acid)	100%; 25 µl	22	48-h patch test; occlusive conditions	Non-irritating	[117]
Chondrus Crispus Powder	Chondrus Crispus Powder (100%)	100%; 0.02 ml	12	24-h patch test; occlusive conditions	Non-irritating	[118]
Corallina Officinalis Extract, Gigartina Stellata Extract, Kappaphycus Alvarezii Extract	Trade name mixture containing water (45.7%), glycerin (40%), *Gigartina stellata* (4.43%), Kappaphycus Alvarezii Extract (5.9%), Corallina Officinalis Extract (3.97%)	10%; 0.02 ml	25	48-h patch test; occlusive conditions	Non-irritating	[119]
Corallina Officinalis Extract	Trade name mixture containing 50% glycerin; 30% water; 18.5 % undaria pinnatifida extract; 1.5% Corallina Officinalis Extract	10%; 160 µl	10	48-h patch test; semi-occlusive conditions	Non-irritating	[120]
Delesseria Sanguinea Extract	Mixture containing Delesseria Sanguinea Extract (0.2 – 4% algae), water, and dipropylene glycol	100%; dose not reported	12	48-h patch test; occlusive conditions	Non-irritating	[18]

Table 14. Dermal irritation and sensitization

Ingredient	Test Substance	Concentration/Dose of the test substance	Test Population/ # of test samples	Procedure	Results	Reference
Furcellaria Lumbricalis Extract	Mixture containing Furcellaria Lumbricalis Extract (0.2 – 4% algae) and water	100%: dose not reported	10	48-h patch test; occlusive conditions	Non-irritating	[21]
Gelidium Cartilagineum Extract	Trade name mixture containing >96% glycerides, mixed decanoyl and octanoyl; <2 % Gelidium Cartilagineum Extract; 1.5-2% 4-cholesten-3-one	10% dilution; 20 µl	10	24-h patch test; occlusive conditions	Non-irritating	[121]
Gelidium Sesquipedale Extract	Trade name mixture containing 48% water; 48% butylene glycol; 4% Gelidium Sesquipedale Extract	5% dilution; 0.02 ml	10	48-h patch test; occlusive conditions	Non-irritating	[122]
Hydrolyzed Corallina Officinalis Extract	Trade name mixture containing >96% water; 0.5-3% Hydrolyzed Corallina Officinalis Extract; 0.16-0.20% sodium methylparaben	100%; 0.02 ml	11	24-h patch test; occlusive conditions	Non-irritating	[123]
Hydrolyzed Corallina Officinalis Extract	Trade name mixture containing >96% water; 0.5-3% Hydrolyzed Corallina Officinalis Extract; 0.8-1.2% phenoxyethanol	100%; 20 µl	11	24-h patch test; occlusive conditions	Non-irritating	[124]
Hypnea Musciformis Extract	Trade name mixture consisting of 72-77% water; 20-70% butylene glycol; 1-3% Hypnea Musciformis Extract; ≤1% potassium gluconate; 0.16-0.2% methylparaben	100%; 0.02 ml	12	24-h patch test; occlusive conditions	Slightly irritating at the 30-min reading (in 7/12 subjects) and non-irritating at the 24-h reading	[72]
Hypnea Musciformis Extract	Hypnea Musciformis Extract in water (specific composition not reported)	15% (0.36% dry matter); dose not reported	11	48-h patch test; occlusive conditions	Non-irritating	[30]
Lithothamnion Calcareum Powder	Trade name mixture consisting of 57-61% Lithothamnion Calcareum Powder. 26-31% mannitol, 9-11% diatomaceous earth, 0.7-1.5% zinc sulfate	100%; 0.02 ml	11	24-h patch test; occlusive conditions	Non-irritating	[125]
Palmaria Palmata Extract	Palmaria Palmata Extract in water (specific composition not reported)	10% (0.75% dry matter); dose not reported	11	48-h patch test; occlusive conditions	Non-irritating	[30]
Polysiphonia Lanosa Extract	Trade name mixture consisting of 67.5% water, 32% Polysiphonia Lanosa Extract	5%; 0.02 ml	11	48-h patch test; occlusive conditions	Non-irritating	[126]
Rhodymenia Palmata Extract	Eye cream containing 0.0375% Rhodymenia Palmata Extract	100%; 0.2 g	38	7-d exposure; semi-occlusive conditions	Non-irritating	[127]
SENSITIZATION						
Human						
Asparagopsis Armata Extract	Product containing 0.325% Asparagopsis Armata Extract	100%; dose not reported	108	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[128]
Asparagopsis Armata Extract	Trade name mixture containing 0.5 –2% Asparagopsis Armata Extract, 56 – 62% water, and 38 – 42% propanediol	3%; 40 µl	104	HRIPT under semi-occlusive conditions	Non-irritating; Non-sensitizing	[73]
Betaphycus Gelatinum Extract	Mixture containing 7% Betaphycus Gelatinum Extract	100%; dose not reported	56	HRIPT under semi-occlusive conditions	Non-irritating; Non-sensitizing	[80]
Chondrus Crispus Extract	Product containing 0.49% Chondrus Crispus Extract	100%; dose not reported	113	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[74]
Corallina Officinalis Extract	Mixture containing Corallina Officinalis Extract (0.2 – 4%), sea water, calcium carbonate, and calcium chloride	100%; dose not reported	103	HRIPT (occlusivity not reported)	Non-irritating; Non-sensitizing	[15]

Table 14. Dermal irritation and sensitization

Ingredient	Test Substance	Concentration/Dose of the test substance	Test Population/ # of test samples	Procedure	Results	Reference
Corallina Officinalis Extract	Blush powder containing 2% Corallina Officinalis Extract moistened with distilled water	dilution not reported; 0.1 – 0.15 g	102	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[79]
Delesseria Sanguinea Extract	Mixture containing Delesseria Sanguinea Extract (0.2 – 4% algae), water, and dipropylene glycol	100%; dose not reported	104	HRIPT (occlusivity not reported)	Non-irritating; Non-sensitizing	[18]
Furcellaria Lumbricalis Extract	Mixture containing Furcellaria Lumbricalis Extract (0.2 – 4% algae) and water	100%; dose not reported	50	HRIPT (occlusivity not reported)	Non-irritating; Non-sensitizing	[21]
Furcellaria Lumbricalis Extract	Mixture containing Furcellaria Lumbricalis (0.2 – 4% algae), sea salt, and water	100%; dose not reported	105	HRIPT (occlusivity not reported)	Non-irritating; Non-sensitizing	[21]
Gelidiella Acerosa Extract	Product containing 0.0028% Gelidiella Acerosa Extract	100%; dose not reported	105	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[75]
Gelidium Cartilagineum Extract	Trade name mixture consisting of >96% glycerides, mixed decanoyl and octanoyl; < 2 % Gelidium Cartilagineum Extract; 1.5-2% 4-cholesten-3-one	100%; 25 µl	50	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[76]
Hydrolyzed Corallina Officinalis Extract	>96% water; 0.5-3% Hydrolyzed Corallina Officinalis Extract; 0.16-0.20% sodium methylparaben	100%; 0.2 ml	51	HRIPT under occlusive conditions	Non-sensitizing	[77]
Hypnea Musciformis Extract	Hypnea Musciformis Extract (specific composition not reported)	15% (0.36% dry matter); dose not reported	100	HRIPT (use of occlusion not reported)	Non-irritating; Non-sensitizing	[30]
Kappaphycus Alvarezii Extract	Trade name mixture consisting of 0.8% Kappaphycus Alvarezii Extract, 79.2% water, and 20% 1,3-butylene glycol	100%; 50 µl	50	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[82]
Palmaria Palmata Extract	Palmaria Palmata Extract in water (specific composition not reported)	25% (1.87% dry matter); dose not reported	58	HRIPT (use of occlusion not reported)	Non-sensitizing	[30]
Porphyra Umbilicalis Extract	Product containing 0.0004% Porphyra Umbilicalis Extract	100%; dose not reported	103	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[78]
Porphyridium Cruentum Extract	Moisturizer containing 0.000545% Porphyridium Cruentum Extract	dilution not reported; 0.1 – 0.15 g	107	HRIPT under occlusive conditions	Non-irritating; Non-sensitizing	[83]

HRIPT = Human Repeat Insult Patch Test; MTT = 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; NR = Not Reported

Table 15. Ocular Irritation Studies

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
IN VITRO					
Trade name mixture containing 0.75% Ahnfeltiopsis Concinna Extract (other components not specified)	100%; 50 µl (liquid) or 50 mg (solid)	2	Test substance was applied to reconstructed cornea epithelium; after application, epithelia was incubated for 90 min	Non-irritating	[70]
An Asparagopsis Armata Extract containing 4% dry algal matter (other components not specified)	100%; dose not reported	NR	Cell viability assessed by using neutral red release assay (PREDISAFE) method	Slightly-irritating	[60]
Mixture containing 98.6% Asparagopsis Armata Extract (4% dry extract), 1% butylene glycol, 0.2% chlorphenesin, and 0.2% parabens/ phenoxyethanol	100%; dose not reported	NR	HET-CAM assay	Non-irritating	[58]
After-shave balm containing 0.8% Chondrus Crispus (other components not specified)	100%; 100 µl	3	MatTek EpiOcular™ MTT assay	Non-irritating	[84]
Trade name mixture containing 3.5% Chondrus Crispus Extract (other components not specified)	100%; 50 µl (liquid) or 50mg (solid)	2	MatTek EpiOcular™ MTT assay	Non-irritating	[71]
Corallina Officinalis Extract (0.2 – 4% algae) in seawater, calcium chloride, and propylene glycol	NR	NR	PREDISAFE assay	Slightly-irritating	[15]
Trade name mixture consisting of 50% glycerin; 30% water; 18.5 % undaria pinnatifida extract; 1.5% Corallina Officinalis Extract	10%; 5 ml	4	HET-CAM assay	Non-irritating	[87]
Mixture containing Delesseria Sanguinea Extract (0.2 – 4%), water, and dipropylene glycol	100%; dose not reported	NR	Neutral red release assay	Non-irritating	[18]
Mixture consisting of Furcellaria Lumbricalis Extract (0.2 – 4%), water, and sea salt	100%; dose not reported	NR	Agar diffusion cytotoxicity assay	Non-irritating	[21]
Trade name mixture consisting of water (45.7%), glycerin (40%), *Gigartina stellata* (4.43%), Kappaphycus Alvarezii Extract (5.9%), Corallina Officinalis Extract (3.97%)	10%; 5 ml	4	HET-CAM assay	Slightly-irritating	[86]
Trade name mixture consisting of 57-61% Lithothamnion Calcareum Powder, 26-31% mannitol, 9-11% diatomaceous earth, 0.7-1.5% zinc sulfate in water	2%, 5%, and 10%; 0.3 ml	4	HET-CAM assay	Moderately irritating at the 10% concentration; non-irritating at the 2 and 5% concentrations	[88]
Trade name mixture consisting of 52% water, 48% Porphyra Umbilicalis Extract	100%; dose not reported	6	HET-CAM assay	Weakly irritating	[63]
Eye cream containing 0.0375% Rhodymenia Palmata Extract	100%; 100 µl	8	MatTek EpiOcular™ MTT assay	Non-irritating	[85]
ANIMAL					
Corallina Officinalis Extract (0.2 – 4% algae) in water	100%; dose not reported	3 rabbits (strain not reported)	Primary ocular tolerance assay	Slightly irritating	[15]
Delesseria Sanguinea Extract (0.2 – 4% algae) in water and dipropylene glycol	NR	3 rabbits (strain not reported)	Primary ocular tolerance assay	Slightly irritating	[18]

HET-CAM = hen's egg test chorioallantoic membrane; MTT = 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazoliumBromide; NR = not reported

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