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

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date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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

The 2018 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Ronald A. Hill, Ph.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth Ph.D. This report was prepared by Lillian C. Becker, former Scientific Analyst/Writer and Priya Cherian, Scientific Analyst/Writer.

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INTRODUCTION

This is a review of the safety of 84 brown algae-derived ingredients as used in cosmetics (Table 1). The ingredients in this review are extracts, powders, juices, or waters derived from one or multiple species of brown algae. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), these brown algae-derived ingredients are most commonly used as skin conditioning agents (Table 2).[1] These ingredients are also reported to be used as absorbents, antioxidants, binders, hair conditioning agents, oxidizing agents, pH adjusters, and viscosity increasing agents.

There are several major groups of algae (as described in "Algae Identification" section). However, this safety assessment focuses only on brown algae. 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 these ingredients are derived, the standard taxonomic practice of using *italics* is followed (e.g., *Agarum cribrosum*). However, when general algal groups are discussed, the phylum name will be used (e.g., brown algae (Phaeophyta)). The term "kelp" is commonly used when referring to brown algae. Kelp are large brown algae that belong to the order Laminariales.[2]

Several brown algae constituents, such as phytosterols,[3] phytosteryl ingredients,[3] and alginic acid[4] were found to be safe as used by the Cosmetic Ingredient Review (CIR) Expert Panel (Panel). The full reports on these ingredients can be accessed on the CIR website (https://www.cir-safety.org/ingredients); therefore, information regarding these ingredients will not be included in this report.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that CIR typically evaluates, is provided on the CIR website (http://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; http://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

The European Chemical Agency (ECHA)[5,6] website provides summaries of data generated by industry, and is cited throughout the report as appropriate. Also referenced in this safety assessment are summary data found in reports, including those published by the European Medicines Agency (EMA),[7,8] the European Food Safety Authority (EFSA) Panel on Dietetic Products, Nutrition and Allergies (NDA),[9] and Food Standards Australia New Zealand (FSANZ).[10,11]

CHEMISTRY

Definitions

The ingredients in this safety assessment are derived from various species of brown algae. "Algae" is not a taxonomic group, but a functional group of convenience.[12] 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, and they are commonly referred to as brown algae (Phaeophyta), green algae (*Chlorophyta*), diatoms (*Bacillariophyta*), chrysophytes (*Chrysophyta*), blue-green algae (*Cyanophya*), red algae (*Rhodophyta*), dinoflagellates (*Pyrrhophyta*), and euglenoids (*Euglenophyta*). The different algal phyla are differentiated by storage products, pigmentation, cell wall constituents, and flagella. A list of the major groups of algae along with their defining characteristics can be found in Table 3.

Brown algae are mostly comprised of large, leathery seaweeds and are classified in about 265 genera with more than 1500 species.[12,13] The actual color varies depending on the proportion of brown pigment (fucoxanthin) to green pigment (chlorophyll). This algal group contains alginic acid and fucoidan in its complex cell walls. General characteristics and the geographic distribution of the specific species of brown algae in this report are presented in Table 4**.**

As with plant-derived ingredients, the constituent composition of these seaweed ingredients can vary widely depending on growing conditions, age of the organisms, local environmental aspects, harvesting conditions, methods of extraction, and many other variables. The concentration of the most abundant carotenoid pigment in brown algae, fucoxanthin, varies remarkably depending on the age of the alga, and the protein content in brown algae varies considerably depending on the season in which it is harvested.[14,15]

Harvesting

Originally, the only source of brown algae was in the wild; but since the mid-twentieth century, demand has exceeded the supply that could be harvested from wild sources, and methods for cultivation have been developed.[16] Consequently, today, commercial brown seaweed comes mainly from farming rather than wild sources. *Laminaria japonica* and *Undaria pinnatifida* are among the most cultivated species of brown algae.[17] Several species, such as *Laminaria japonica*, are grown on suspended ropes in the ocean.[16] Repeated harvesting of *Macrocystis pyrifera* over a 3-month period did not significantly impact tissue chemical properties (i.e. alginate yield; viscosity and strength; nutritional quality, such as protein, carbohydrate, lipid, crude fiber, ash, and energy content; and tissue carbon/nitrogen ratios).[18]

Physical and Chemical Properties

Physical and chemical properties of Ascophyllum Nodosum Extract, Ascophyllum Nodosum Powder, and Ecklonia Cava Extract are presented in Table 5. Using the sieve method, 93.5% of the particle sizes of Ascophyllum Nodosum Extract, as a fully dried extract, were less than 0.250 mm and greater than 0.045 mm.[6]

Method of Manufacture

Numerous methods of manufacture are provided in Table 6.[9,19-31] Several of these methods have a target constituent or composition (e.g., high in fucoidan). The characterization of the final extract is provided in the table.

Arsenic is a constituent of concern in certain brown algae [see Constituents of Concern].[10,11,32,33] There are methods to remove the arsenic, including extraction with water, methanol, or water/methanol mixtures accompanied with sonication or mechanical agitation.[34] Extraction with microwave-assisted heating and accelerated solvent extraction systems are described in the literature.[34] Soaking the algae in water at room temperature followed by simmering in the water is shown to be effective for removing inorganic arsenic.[35] Another variation entails repeated boiling in seawater, replacing the water three times, after initial soaking.[32] Soaking the algae in a simmering 4% acetic acid or a 4% sodium hydrogen carbonate aqueous solution has also been shown to remove arsenic.[36]

Composition

There have been no data found or submitted on the composition of any of the ingredients in this report as used in cosmetics specifically. However, some constituents and constituent groups that are found in brown algae in general are presented in Table 7; included are alkaloids, laminarins, pheromones, phytohormones, and terpenoids, amino acids, betaines, and characteristic pigments such as chlorophyll a and c, β-carotene, fucoxanthin, and several other xanthophyls.[37] The compositions of *Ascophyllum nodosum*, *Fucus vesiculosus* and *Laminaria digitate* are provided in **Error! Reference source not found.**

Sterols are also found in brown algae.[38,39] Sterols reported to be in *Cystoseira tamariscifolia*, *Fucus spiralis*, and *Sargassum vulgare* are provided in Table 9.

Methanol, hexane, and chloroform extracts from *Cystoseira compressa* were examined for flavonoid and phenolic content.[40] The flavonoid content of the methanol, hexane, and chloroform extract were 0.291 ± 0.02, 0.88 ± 0.07 and 0.804 ± 0.07 mg/g, respectively. The phenolic content of hexane (1.541 ± 0.09 mg/g) was considerably higher than the phenolic content of the methanol (0.161 ± 0.08 mg/g) and chloroform (0.45 ± 0.04 mg/g) extracts.

Constituents of ethanolic extracts of *Fucus spiralis* and *Sargassum vulgare* are presented in Table 10. The constituent with the highest concentration in both extracts is vaccenic acid (21,690 and 2848 ppm, respectively).[41]

The composition of a water/propylene glycol extract of *Laminaria japonica* is provided in Table 11.[28] The compositions of extracts of *Laminaria japonica*[26] that are produced via enzyme hydrolysis are presented in Table 12.

The specifications for an alcohol extract of *Ecklonia cava*, as a food/dietary supplement, include a combined phlorotannin content of 90.0 ± 5.0%; the content of dieckol, a specific phlorotannin, is 6.6% to 9.9% (Table 13).[9] The extract is to contain no insoluble substances, and it is reported to contain calcium (4800 ± 400 mg/kg), magnesium (1300 mg/kg), potassium (700 ± 200 mg/kg), and iodine (220 ± 40 mg/kg).

An *Undaria pinnatifida* extract rich in fucoidan (extraction method presented in Table 6) was characterized as having 27% uronic acid, 53% monosaccharides, and 7.4% sulfate.[31] Major monosaccharides included 54% fucose and 35% galactose. The minor monosaccharides were 3% rhamnose, 4% arabinose, and 1% xylose, glucose, and mannose.

A desalinated *Undaria pinnatifida* powder was reported to consist of 532 mg/g dietary fiber, mostly in the form of alginates, and 209 mg/g protein.[42] The composition profile is presented in Table 14.

Impurities/Constituents of Concern

Arsenic – Inorganic

Arsenic, usually in the form of arsenosugars, is a natural constituent of some brown algae, including *Ecklonia radiate*, *Laminaria japonica*, and *Sargassum fusiforme*.[10,11,26,33,43] The amount of arsenic is inconsistent due to varied uptake of inorganic arsenic by brown algae varieties and the influence of external factors (e.g., temperature, season, and pH) on the degree of uptake. Algae contain greater inorganic arsenic levels as a proportion of the total arsenic (e.g., 60% to 73%) than many other foods. The amounts of arsenic that have been measured in various brown algae are presented in Table 15. The different arsenic-containing moieties found in four brown algae species are presented in Table 16. A comparison of the amount of arsenic found in *Laminaria japonica* and a *Laminaria japonica* extract (equivalence to cosmetic ingredients not confirmed) is presented in Table 17.

Heavy Metals

Brown algae exhibit an affinity for heavy metals, which are believed to be absorbed from the water column.[37,44] Heavy metal concentrations in algae are strongly dependent on environmental parameters of the sampling sites (e.g., salinity, temperature, pH, light, nutrient concentrations, oxygen, etc.) and the structural differences among the algae. The seaweeds also absorb heavy metals from the sediment.[45,46] An overview of the amount of heavy metals found in brown algae species can be seen in Table 18.

An edible, phlorotannin-rich, ethanol extract of *Ecklonia cava* has specifications issued by the European Commission.[9] According to the Commission, this extract must contain < 3 mg/kg lead, < 0.1 mg/kg mercury, < 3 mg/kg cadmium, < 25 mg/kg arsenic, and 150 - 650 mg/kg iodine.

Phthalates

Dibutyl phthalate (DBP) and di-(2-ethylhexyl) phthalate (DEHP) have been shown to occur naturally in *Undaria pinnatifida* and *Laminaria japonica*.[47]

USE

Cosmetic

The safety of the cosmetic ingredients included in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetic 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 surveys conducted by the Personal Care Products Council (Council), of maximum reported use concentration by product category.

According to VCRP survey data received in 2018, Fucus Vesiculosus Extract is reported to be used in 287 formulations (201 in leave-on formulations, 75 in rinse-off formulations, and 11 diluted for the bath; Table 19.[48] Laminaria Digitata Extract is reported to be used in 235 formulations, Macrocystis Pyrifera (Kelp) Extract in 188 formulations, and Laminaria Saccharina Extract is used in 132 formulations. All other in-use ingredients are reported to be used in 77 formulations or fewer.

Ascophyllum Nodosum Extract was reported in the VCRP as Ascophyllum Nodosum (Seaweed) Extract and Fucus Vesiculosus Extract was reported as Fucus Vesiculosus (Bladderwrack) Extract. Laminaria Saccharina Extract is reported in the VCRP as Saccharina Latissima (Kelp) Extract; the accepted scientific name for *Laminaria saccharina* is *Saccharina latissima*. There were also entries in the VCRP for ingredients that may be related to the listed brown algae-derived ingredients: kelp (24 uses), kelp extract (15 uses), Laminaria extract (4 uses), Phaeophyceae (brown algae; 4 uses), and seaweed extract (82 uses). It is not known to what extent these erroneous names are connected to any of the ingredients in this report.

The results of the concentration of use surveys conducted by the Council in 2015 and 2016 indicate Laminaria Digitata Powder has the highest reported maximum concentration of use; it is used at up to 40% in face and neck formulations.[49,50] Macrocystis Pyrifera (Kelp) Extract is reported to be used at up to 36.4% in eye lotions. The rest of these ingredients are reported to be used at 6% or less.

In some cases, reports of uses were received in the VCRP, but concentration of use data were not provided. For example, Ascophyllum Nodosum Powder is reported to be used in 4 cosmetic formulations, but no use concentration data were reported. In other cases, no uses were reported in the VCRP, but concentration of use data were reported in the industry survey; Fucus Vesiculosus had no reported uses in the VCRP, but a use concentration in shampoos, moisturizing formulations, and suntan formulations 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 ingredients not in use according to 2018 VCRP data and the 2015 and 2016 Council surveys are listed in Table 20.

Several of these ingredients are used in formulations that are used near the eye (e.g., Macrocystis Pyrifera (Kelp) Extract at up to 36.4% in eye lotion and Fucus Vesiculosus Extract in mascara at up to 5%), incidentally ingested (e.g., Macrocystis Pyrifera (Kelp) Extract in lipsticks at up to 0.079%), and in formulations that come in contact with mucous membranes (e.g., Fucus Vesiculosus Extract and Laminaria Digitata Extract at up to 5% in bubble baths and Laminaria Japonica Extract and Macrocystis Pyrifera (Kelp) Extract at up to 5% in bath oils, tablets and salts).

Additionally, some of the brown algae-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Macrocystis Pyrifera (Kelp) Extract is reported to be used at up to 0.79% in face and neck 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.[51,52] 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.[53,54] Laminaria Japonica Extract and Macrocystis Pyrifera (Kelp) Extract were reported to be used in face powders at concentrations up to 0.0035%. Conservative estimates of inhalation exposures to respirable particles during the use of loose-powder cosmetic products are 400- to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[55-57]

None of the brown algae-derived ingredients named in this report are restricted from use in any way under the rules governing cosmetic products in the European Union.[58]

Non-Cosmetic

Brown seaweeds are consumed around the world and come mostly, but not only, from the *Laminaria*, *Undaria*, and *Hizikia* species.[16] According to the US FDA, brown algae (i.e., several species of seaweeds that are harvested principally in coastal waters of the northern Atlantic and Pacific oceans) 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 (GMP). [21CFR184.1120] "Kelp" (the dehydrated, ground product prepared from *Macrocystis pyrifera, Laminaria digitata, Laminaria saccharina*, and *Laminaria cloustoni*) is approved as a food additive for direct addition to food for human consumption as a source of iodine or as a dietary supplement. [21CFR172.365] In New Zealand, Japan and other Asian countries, dried sea kelp is a common food; the exact species of kelp used varies according to location.[16] The EFSA NDA Panel concluded that an alcohol extract of *Ecklonia cava* is safe for the use in food supplements at a maximum intake level of 163 mg/day for adolescents from 12 to 14 years of age, 230 mg/day for adolescents above 14 years of age, and 263 mg/day for adults.[9]

In animal drugs, feeds, and related products, brown algae (kelp; *Laminaria* spp. and *Nereocystis* spp.) are GRAS as natural substances [21CFR582.30] and as solvent-free natural extractives [21CFR582.40] used in conjunction with spices and other natural seasonings and flavorings.

In the US, "kelp" is present in OTC medications for weight loss. [21CFR310.545] However, there are inadequate data to establish a general recognition of the safety and effectiveness of this ingredient for that specified use. Several other sources refer to the use of *Fucus vesiculosus* for weight loss.[59,60]

Pastes of seaweed, made by cold grinding or freeze crushing, are used in thalassotherapy, where the pastes are applied to the body and then warmed under infrared radiation.[16] This treatment, in conjunction with seawater hydrotherapy, is said to provide relief for rheumatism and osteoporosis. In folk medicine, preparations of *Fucus vesiculosus* are used to treat hypothyroidism, iodine deficiency, arteriosclerosis, digestive disorders, menstrual abnormalities, cellulite, and sprains.[59,61] As herbal folk medicine, *Laminaria hyperborean* is used for thyroid regulation, and *Macrocystis Pyrifera* is used to treat thyroid conditions, anemia in pregnancy, and hypertension, weight loss, and as an immunity booster.[59]

Brown algae have been used as fertilizers and soil conditioners (*Ascophyllum*, *Sargassum*, *Ecklonia*, and *Fucus* species), animal feed for sheep, cattle, horses, pigs, and chickens (*Alaria esculenta*, and *Ascophyllum* and *Laminaria* species), feed and feed binder for fish and abalone (*Macrocystis pyrifera*), and biomass fuel (*Macrocystis pyrifera*), and they have been used for waste water/effluent treatment and removal of heavy metals (*Sargassum*, *Laminaria*, and *Ecklonia* species).[16,37] Brown algae are used as biomonitors for heavy metal pollution in estuarine and coastal waters worldwide, and to evaluate the quality of their surrounding environment.[44]

TOXICOKINETIC STUDIES

Obtaining data on the toxicokinetics of uncharacterized, complex mixtures would be impractical, as is the case with many botanical ingredients. No toxicokinetics studies were discovered in the published literature, and no unpublished data were submitted.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

No acute dermal or inhalation toxicity studies were discovered in the published literature, and no unpublished data were submitted. Acute oral toxicity studies summarized below are presented in Table 21**.**

Oral

Cystoseira Compressa Extract was not toxic to mice when given a single dose of up to 2000 mg/kg by gavage.[40] The oral LD_{50}s of two Fucus Vesiculosus Extracts were 1000 and 500 mg/kg for male mice and between 1000 and 2000 mg/kg and < 750 mg/kg for female mice.[23] In rats (sex not stated), the oral LD_{50}s of two Fucus Vesiculosus Extracts were between 1000 and 2000 mg/kg for one extract and > 2000 mg/kg for the second extract.[23] There were no signs of toxicity when rats were given a single dose of up to 4000 mg/kg Laminaria Japonica Extract via oral gavage.[62] Sargassum Fulvellum Extract and Sargassum Thunbergii Extract were not toxic to mice that were given a single dose of 5 g via oral gavage.[63]

Short-Term, Subchronic, and Chronic Toxicity Studies

No repeated dose dermal or inhalation toxicity studies were discovered in the published literature, and no unpublished data were submitted. Short-term, subchronic, and chronic oral toxicity studies summarized below are presented in Table 22.

Oral

Ascophyllum Nodosum was not toxic when it was fed to pigs via a 10% oral diet for 23 days, or rats fed a 15% diet for 4 weeks. Ecklonia Cava Extract was not toxic to rats dosed with up to 3000 mg/kg via oral gavage once daily in rats, and twice daily in dogs for 13 weeks.[9,21] An enzyme extract of Ecklonia Cava Extract (starting at doses of 2000 mg/kg) administered by gavage for 2 weeks caused reduced ovary and brain weights in female rats.[21] Hepatic effects in rats were observed when animals were dosed with 2000 mg/kg/day via oral gavage of an alcohol Ecklonia Cava Extract for 4 weeks. When rats were dosed with the same extract in doses of 1500 mg/kg/day for 13 weeks, there were also effects on body weight gain and organ weights (the hepatic effects resolved after 4 weeks recovery).[9]

Increased liver weights were apparent when two ethanol Fucus Vesiculosus Extracts (starting at doses 200 mg/kg/day) were administered by gavage for 4 weeks in male rats.[23] While consuming high-fat diets, there were no adverse effects caused by alcohol Ecklonia Cava Extract when mice were given doses of up to 5 mg/day via gavage for 4 weeks.[64] An ethanol Laminaria Japonica Extract (up to 400 mg/kg) administered by gavage for 6 weeks caused decreased body weight gain, fat-pad weights, and serum and hepatic lipid levels in rats.[27] Vomiting was the only adverse effect when Ecklonia Cava Extract in capsules was orally administered (in increasing amounts up to 1000 mg/kg over 8 days) to dogs.[9] A *Ecklonia cava* powder (up to 0.15%; inference for Ecklonia Cava Extract and Ecklonia Cava Water) administered in feed for 28 days was not toxic to weanling pigs.[65] An *Undaria pinnatifida* extract (hydrolyzed in hydrochloric acid) administered orally for 28 days was not toxic to rats up to 1000 mg/kg/day, but alanine aminotransferase (ALT) and triglyceride levels in males and high-density lipoprotein (HDL) cholesterol in females increased at 2000 mg/kg/day.[31]

In rats, Cladosiphon Okamuranus Extract doses of 1200 to 4000 mg/kg given once a day for three months via oral gavage caused a dose-dependent increase in clotting time and decrease in alkaline phosphatase (ALP) that was not observed with lower doses. There were no other adverse effects reported.[19]

Laminaria Japonica Powder (up to 5%) was incorporated in the feed of mice from the age of 7 weeks until death. There were no dose-dependent effects on the lifespan of mice.[29] Undaria Pinnatifida Extract administered via drinking did not cause any toxic effects in rats when administered for 32 weeks.[66] Undaria Pinnatifida Extract (up to 5%) incorporated into feed of rats for 36 weeks did not cause any toxic effects.[29] The no observable adverse effect level (NOAEL) of a Laminaria Japonica Extract administered to rats by gavage for 6 months was 300 mg/kg/day.[62] In females, a decrease in aspartate aminotransferase (AST) was observed starting at 300 mg/kg/day and, at 2500 mg/kg/day, there was decreased serum glucose concentration. After a 1-month recovery period, these changes in glucose and AST returned to baseline.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No DART studies were discovered in the published literature, and no unpublished data were submitted.

GENOTOXICITY STUDIES

The in vitro and in vivo genotoxicity studies summarized below are presented in Table 23.

In Vitro

Ascophyllum Nodosum Extract was not genotoxic in an Ames assay (up to 5000 µg/plate), a mammalian cell gene mutation test (up to 500 µg/ml), and chromosome aberration assays (up to 5 mg/ml); in the mammalian cell gene mutation test, Ascophyllum Nodosum Extract was genotoxic to Chinese hamster ovary (CHO) cells starting at 1500 µg/ml.[6] Cystoseira Compressa Extract (up to 5 mg/plate) was not genotoxic in an Ames assay.[40] Ecklonia Cava Extract was not genotoxic in Ames assays (up to 5000 µg/plate) and chromosome aberration assays (up to 350 µg/plate).[9,21] Aqueous Fucus Vesiculosus Extract was not genotoxic in a chromosome aberration assay (up to 1 mg/ml) and a comet assay (up to 1 mg/ml).[67] Laminaria Japonica Extract (up to 5000 µg/plate) was not mutagenic in an Ames assay and a chromosome aberration assay.[26] Undaria Pinnatifida Extract was not genotoxic in Ames assays (up to 5000 µg/plate)[31,68,69] and chromosome aberration assays (up to 5000 µg/ml).[68,69]

In Vivo

Ecklonia Cava Extract was not genotoxic in micronucleus assays up to 3000 mg/kg.[9,21] Laminaria Japonica Extract and Undaria Pinnatifida Extract were not genotoxic in micronucleus assays at up to 2000 mg/kg.[26,48,68,69]

CARCINOGENICITY STUDIES

No carcinogenicity studies were discovered in the published literature, and no unpublished data were submitted.

Tumor Promotion

Tumor promotion studies summarized below are presented in Table 24. None of the brown algae-derived ingredients tested were tumor promoters, but decreased the number, incidence, size of tumors in rats and mice.

Dermal

Mice were treated dermally with a single dose of 7,12-dimethylbenz[a]anthracene (DMBA; a carcinogen) followed by twice weekly treatments with 12-*O*-tetradecanoylphorbol-13-acetate (TPA; a tumor promotor) or Undaria Pinnatifida Extract (1 mg).[70] The mice treated with Undaria Pinnatifida Extract had a delayed appearance of skin tumors (14 vs 8 weeks) and fewer tumors (average 0.2 vs 3.7) compared to the TPA-treated mice.

Oral

Rats injected with azoxymethane (AOM; a carcinogen) and then fed a diet containing Hizikia Fusiforme Extract (2% and 6%) had a reduced number of colorectal tumors (21 vs 58) compared to rats injected with AOM and fed a normal diet.[71] A *Saccharina angustata* powder (5%; inference for Saccharina Angustata Extract) in feed delayed the appearance and reduced the incidences of mammary tumors in rats orally administered DMBA.[72]

Rats administered *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG; a carcinogen) followed by Sargassum Pallidum Extract (0, 400, 600 and 800 mg/kg/day) in drinking water for 8 weeks had decreased inflammatory responses; serum IL-6, IL-1β, and TNF-α levels and concentration of serum and gastric mucosa malondialhehyde (MDA; an oxidant) were decreased in a dose-dependent manner.[73] In rats administered Undaria Pinnatifida Powder (0, 1.0% or 5.0% in feed) for 8 weeks after oral administration of DMBA, the mean combined weight of all mammary tumors of each rat in treatment groups was lower than that in the control group (approximately 7 vs 20 g).[74] Undaria Pinnatifida Extract (100% as drinking water) for 32 weeks reduced the incidence of mammary tumors (22% vs 100%) after female rats were orally administered DMBA.[66]

OTHER RELEVANT STUDIES

Estrogenic Effects

In Vitro

Fucus vesiculosus extract

Human granulosa cells (obtained from 8 women) were treated with a water:ethanol (1:1) *Fucus vesiculosus* extract (25, 50, or 75 µmol/l) for 9 days.[75] Ethanol (50%) served as the vehicle control. At 50 and 75 µmol/l, the extract significantly reduced 17-β-estradiol levels in human granulosa cells and also competed with estradiol (E2) and progesterone for binding to their receptors.

Affinity of this extract for estrogen receptor (ER)α, ERβ, and progesterone receptor (PR)-B was determined by radiometric competitive binding assays.[75] Dried extract (0.5, 5, or 50 µmol/l final concentration) was re-solubilized in dimethyl sulfoxide and combined with ERα or ERβ and 0.5 nmol/l estradiol. Non-specific binding was estimated in the presence of 1 µmol/l diethylstilbesterol. To test PR-B binding, the extract was incubated with PR-B and 1.4 nmol/l radiolabeled progesterone. Non-specific binding was estimated in the presence of 1 µmol/l progesterone. The extract competed for and bound to ERα (IC_{50} = 42.2 µmol/l), ERβ (IC_{50} = 31.8 µmol/l), and PR-B (IC_{50} = 31.8 µmol/l), with a slightly greater affinity for ERβ. The inhibition of progesterone production was less prominent, and there was no concentration-response relationship. In contrast, there was a concentration-dependent occupancy of the estrogen and progesterone receptors. Compounds found in *Fucus vesiculosus* could act as estradiol antagonists by decreasing the affinity of either ERα or ERβ for its ligand.

In competitive radio-ligand binding assays, aromatase activity was estimated by measuring the incorporation of tritium from androstenedione into water in the presence or absence of a *Fucus vesiculosus* extract (10, 50, or 100 µmol/L).[75] Aromatase activity following treatment of human luteinized granulosa cells (hLGCs) with this extract did not change.

A chemically activated luciferase reporter (CALUX®) assay was used to determine the effect of an aqueous *Fucus vesiculosus* extract on activation of the ER.[76] Aromatase enzymatic activity was measured to determine the potential effect of this extract on E2 biosynthesis. In co-treatments with E2, this extract (2%) reduced the activation of the luciferase reporter by up to 50%, exhibiting potent ER antagonistic effects. The effect of this extract (0 to 2%) on aromatase activity was measured using recombinant human CYP19 enzymatic hydrolysis of the fluorescent substrate, 7-methoxy-4-rifluoromethyl coumarin, in a 96-well plate. Ketoconazole was used as the positive marker of aromatase inhibition. This extract inhibited aromatase activity (IC_{50} 2.0%). ER-dependent and -independent cancer cell lines showed significantly decreased viability with increasing *Fucus vesiculosus* extract concentrations; altered morphological features suggested apoptosis and autophagy. The cell line-specific sensitivity suggests that *Fucus vesiculosus* extract was not toxic at up to 2%, but instead induces cell death through modulated pathways.

Animal

Fucus vesiculosus powder

Female Sprague-Dawley rats (n = 8), that had two confirmed normal estrous cycles, were administered a *Fucus vesiculosus* powder (0, 175, or 350 mg/kg/day) on an apple wedge daily for 4 weeks.[75] Vaginal smears were obtained and daily logs were maintained to monitor estrous cycling. No adverse effects were observed during the course of the experiment. Administration of this powder resulted in a statistically-significant, dose-dependent increase in the length of the estrous cycle in the treated rats. In the control group, the mean number of days of the estrous cycle was 4.3 ± 0.96 days compared to 5.4 ± 1.7 days in the low-dose group and 5.9 ± 1.9 days in the high-dose group. Treatment with this powder caused an overall 100% increase in the mean length of the diestrus phase of the estrous cycle. The mean number of days in diestrus was 0.97 ± 0.22 among the controls compared to 1.4 ± 0.54 in the low-dose group and 2.1 ± 0.88 days in the high-dose group. Treatment had no significant effect on the number of days in estrus, proestrus, or metestrus during the mean estrous cycle. After treatment was stopped, five rats stopped normal estrous cycling; one remained in estrus and four in diestrus.

Blood samples were collected from female Sprague-Dawley rats (n = 19) before treatment, and at 2 and 4 weeks of the oral administration of this powder (0 or 175 mg/kg/d) on apple wedges.[75] At 2 weeks, mean serum 17β-estradiol levels were reduced from 48.9 ± 4.5 to 40.2 ± 3.2 ng/l and, after 4 weeks, reduced the levels from baseline to 36.7 ± 2.2 ng/l (25% decrease), suggesting an effect of dosing over time. Serum progesterone levels between controls and the treatment groups did not differ.

Blood samples were collected from female Sprague-Dawley rats (n = 8), that had naturally high circulating estradiol levels (≥ 50 µg/l), before, and after 1 week of the oral administration of this powder (350 mg/kg/day) on apple wedges.[75] Median serum 17-β-estradiol levels decreased by 38%. The range in reduction of serum 17-β-estradiol levels in 6 of the rats was 25% to 58%, whereas 2 rats had levels similar to their baseline levels. Progesterone levels were not significantly affected following this treatment. This could be due to the fact that in the studies with rats the blood samples were collected in the morning, and in the morning the 17-β-estradiol levels were at their peak but the progesterone levels were not.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Animal

Ascophyllum nodosum extract

A dermal irritation assay of an *Ascophyllum nodosum* extract (0.5 g in water; dose not specified) was conducted in accordance with the Organisation for Economic Co-operation and Development Guideline (OECD GL) 404 (Acute Dermal Irritation/Corrosion) using New Zealand White rabbits (n = 3 males).[6] The test substance was administered in three patches to the shaved backs of the rabbits under semi-occlusion for 3 min (patch 1), 1 h (patch 2), and 4 h (patch 3). There were no signs of irritation after the removal of patch 1 from one rabbit; patch 2 was then applied to the same rabbit. There were no signs of irritation after patch 2 was removed; patch 3 was then applied to all three rabbits. The test site was examined at 1, 24, 48, and 72 h after the removal of the last patch. The primary irritation index was 0 out of 8 at each observation.

Human

Laminaria japonica extract

A patch test on a skin cream containing a 50/50 aqueous/propylene glycol extract of *Laminaria japonica* (10%; 20 mg) was conducted.[28] The cream was administered to the forearms of subjects (n = 25) in Finn chambers for up to 48 h and scored for irritation 6 h after patch removal. The test substance had a score of 0 and was considered to be non-irritating.

Sensitization

No sensitization studies were discovered in the published literature, and no unpublished data were submitted.

Photoprotection

Sargassum muticum extract

The effect of a *Sargassum muticum* extract (SME) against cell death induced by UVB radiation was studied.[77] Cell viability was 61% in UVB (150 mJ/cm^2) irradiated cells and 70% in UVB-irradiated cells treated with SME. Decreased numbers of apoptotic bodies as well as DNA fragmentation was apparent in cells exposed to SME and UVB versus UVB exposure alone.

OCULAR IRRITATION STUDIES

Ascophyllum nodosum extract

An ocular irritation test was conducted on an *Ascophyllum nodosum* extract (100 mg) in accordance with OECD GL 405 (Acute Eye Irritation/Corrosion) using New Zealand White rabbits (n = 3 males).[6] The test substance was instilled into one eye of each rabbit; the other eye served as the control. After 1 h, both eyes were washed with water. The eyes were examined at 1, 24, 48, and 72 h and 7 days after instillation. The maximum irritation score was 6.7 out of 8 at 1 h post-instillation; the score decreased to 0 by day 7, which indicated that the induced changes were reversible, and thus, the effects of the test substance were classified as 'irritation' and not as 'corrosion.' The test substance was rated as a mild ocular irritant.

CLINICAL STUDIES

Case Reports

Oral case reports regarding brown-algae derived supplements are presented in Table 26.

Clinical Trials

Oral

Clinical trials summarized below are presented in Table 27.

In an oral clinical trial in which an *Ascophyllum nodosum* powder (0.5g/d) was administered to healthy female subjects, median urinary iodine concentrations increased from 78 mg/l to 140 mg/l, and thyroid-stimulating hormone (TSH) concentrations slightly, but remained within the normal range.[78] There were no adverse events reported. Administration of an alcohol extract of *Ecklonia cava* (400 mg/day) to subjects with hypercholesterolaemia for 12 weeks did not have an effect on hematology, clinical chemistry, or urinalysis parameters; however, one instance (2.2%) each of nausea, dyspepsia, diarrhea, and alopecia were reported.[9,79] A phlorotannin-rich extract of *Ecklonia cava* (0, 72, or 144 mg/day) was administered for 12 weeks to overweight patients in a randomized, double-blind study. Hematological and clinical chemistry did not reveal any adverse effects; the 144 mg/day group showed decreases in serum glucose and systolic blood pressure (SBP).[9] Administration of capsules containing a desalinated *Undaria pinnatifida* powder (average intake estimated to be 3.3 g per day) to hypertensive subjects for 8 weeks resulted in a decrease in the average SBP, diastolic blood pressure (DBP), and total cholesterol; adverse effects included two cases of indigestion and one case of diarrhea, both of which resolved quickly without treatment.[42]

Three pre-menopausal women with irregular menstrual cycles were administered a *Fucus vesiculosus* powder.[80] Subject number 1 was 43 years old with hypermenorrhea, polymenorrhea, dysmenorrhea, luteal phase deficiency, and endometriosis. Subject number 2 was 42 years old with hypermenorrhea, polymenorrhea, and dysmenorrhea. Subject number 3 was 21 years old with hypermenorrhea, dysmenorrhea, and endometriosis. Menstrual cycles were tracked for three cycles and serum 17β-estradiol and progesterone levels were measured before treatment started. Then the women were administered this powder in capsules (700 mg/day) for two menstrual cycles. Serum 17-β-estradiol and progesterone levels were measured again. Subject 2 stopped treatment at this point and subjects 1 and 3 continued treatment with a greater dose of this powder (1400 mg/day) for two more cycles. This powder increased the menstrual cycle length and reduced the days of menstruation in a dose-dependent manner Table 25). An increase in the average menstrual cycle length and a decrease in the number of menstruating days was noted in all subjects. In subject 1, the plasma estradiol levels were decreased (before: 626 ± 91 pg/ml; low dose: 164 ± 30 pg/ml; high dose: 92.5 ± 3.5 pg/ml) and the progesterone levels were increased (before: 0.58 ± 0.14 ng/ml; low-dose: 8.4 ± 2.6 ng/ml; high-dose: 16.8 ±0.7 ng/ml).[80]

Use Studies

Fucus vesiculosus extract

A gel formulation containing 1% of an aqueous extract of *Fucus vesiculosus* (0.2 ml) was tested in a double-blind, placebo-controlled experiment.[24] Female subjects (n = 10) applied the gel to one cheek at least twice per day (morning and evening) for 5 weeks. The same gel, without the extract, was applied to the other cheek. The skin was examined before the experiment began, daily, and after the experiment ended. There were no signs of erythema or edema during the experiment.

SUMMARY

This is a review of the safety of 85 brown algae-derived ingredients as used in cosmetics. The ingredients in this review are extracts, powders, juices, or waters derived from one or multiple species of brown algae and may be derived from the whole or a defined part of the seaweed. "Brown algae" is a common name for seaweeds of the class *Phaeophyta*, which have an abundance of xanthophyll pigments and are a known source of alginate. The most frequently reported function of brown algae in cosmetics is as a skin-conditioning agent; other reported functions include absorbent, antioxidant, binder, hair

conditioning agent, oxidizing agent, and viscosity increasing agent.

Extraction methods and solvents vary, depending on the desired composition of the final ingredient. Powders, however, are generally the dried algae pulverized by milling. Inorganic arsenic, usually in the form of arsenosugars, is a natural constituent of brown algae and the amount in the harvested algae can be reduced by several methods. In addition to arsenic, brown algae exhibit an affinity for heavy metals and uptake is strongly dependent on environmental parameters.

According to the VCRP survey data received in 2018, Fucus Vesiculosus Extract is reported to be used in 287 formulations (201 in leave-on formulations, 75 in rinse-off formulations, and 11 diluted for the bath). Laminaria Digitata Extract is reported to be used in 235 formulations and Macrocystis Pyrifera (Kelp) Extract in 188 formulations. All other in-use ingredients are reported to be used in 132 formulations or fewer. The results of the concentration of use surveys conducted by the Council in 2015 and 2016 indicate Laminaria Digitata Powder has the highest reported maximum concentration of use; it is used at up to 40% in face and neck formulations. Macrocystis Pyrifera (Kelp) Extract is reported to be used at up to 36.4% in eye lotions. The rest of these ingredients are reported to be used at 6% or less.

In animal drugs, feeds, and related products, brown algae (kelp; *Laminaria* spp. and *Nereocystis* spp.) are GRAS as natural substances and as solvent-free natural extractives used in conjunction with spices and other natural seasonings and flavorings.

Acute oral administration of brown algae extracts was not toxic to mice, rats, and dogs. Cystoseira Compressa Extract was not toxic to mice up to 2000 mg/kg by gavage. Ecklonia Cava Extract was not toxic to rats and dogs up to 3000 mg/kg by gavage. The oral LD_{50}s of two different Fucus Vesiculosus Extracts were 500 mg/kg and greater for mice and rats. There were no signs of toxicity at up to 4000 mg/kg Laminaria Japonica Extract orally administered to rats. Sargassum Fulvellum Extract and Sargassum Thunbergii Extract (both at 5 g) administered by gavage were not toxic to mice.

In oral short-term and subchronic studies, there were some adverse effects observed. In rats, Cladosiphon Okamuranus Extract (1200 to 4000 mg/kg by gavage) caused a dose-dependent increase in clotting time and decrease in ALP; there were no other adverse effects reported. An enzyme extract of Ecklonia Cava Extract (starting at 2000 mg/kg) administered by gavage for 2 weeks caused reduced ovary and brain weights in female rats. Hepatic effects in rats were observed in an alcohol Ecklonia Cava Extract at 2000 mg/kg/day for 4 weeks and at 1500 mg/kg/day when administered for 13 weeks (the hepatic effects resolved after 4 weeks of recovery). There were increased liver weights in two ethanol Fucus Vesiculosus Extracts (starting at 200 mg/kg/day) administered by gavage for 4 weeks in male, but not female rats. Vomiting was the only adverse effect when Ecklonia Cava Extract capsules (in increasing amounts up to 1000 mg/kg over 8 days) were orally administered to dogs.

In other oral short-term and subchronic studies, there no adverse effects observed. Ascophyllum Nodosum was not toxic to pigs for 23 days or to rats for 4 weeks administered in feed at up to 10% and 15%, respectively. While consuming high-fat diets, there were no adverse effects caused by alcohol Ecklonia Cava Extract (up to 5 mg/day) administered to mice by gavage daily for 4 weeks and an ethanol Laminaria Japonica Extract (up to 400 mg/kg) administered by gavage for 6 weeks caused decreased body weight gain, fat-pad weights, and serum and hepatic lipid levels in rats. A *Ecklonia cava* powder (up to 0.15%; inference for Ecklonia Cava Extract and Ecklonia Cava Water) administered in feed for 28 days was not toxic to weanling pigs. An orally administered *Undaria pinnatifida* extract for 28 days was not toxic to rats up to 1000 mg/kg/day, but ALT and triglyceride levels in males and HDL cholesterol in females increased at 2000 mg/kg/day.

In a chronic oral toxicity study, the NOAEL of a Laminaria Japonica Extract administered to rats by gavage for 6 months was 300 mg/kg/day. In females, a decrease in AST was observed starting at 300 mg/kg/day and, at 2500 mg/kg/day, there was decreased serum glucose concentration; all effects returned to baseline after a 1-month recovery. Laminaria Japonica Powder incorporated into feed did not affect the lifespan of mice at up to 5%. In rats, Undaria Pinnatifida Extract administered as drinking water at 100% for 32 weeks and incorporated into the feed (at up to 5%) for 36 weeks did not cause any toxic effects.

In genotoxicity assays of several of the brown algae-derived ingredients, all results were negative with the exception of an Ascophyllum Nodosum Extract in one mammalian cell gene mutation test in which the extract was genotoxic starting at 1500 µg/ml in CHO cells. Ascophyllum Nodosum Extract was not genotoxic in an Ames assay and a mammalian cell gene mutation test (up to 500 µg/ml), and in chromosome aberration assays (up to 5 mg/ml). Cystoseira Compressa Extract (up to 5 mg/plate) was not genotoxic in an Ames assay. Ecklonia Cava Extract was not genotoxic in Ames assays (up to 5000 µg/plate) and chromosome aberration assays (up to 350 µg/plate). Aqueous Fucus Vesiculosus Extract was not genotoxic in a chromosome aberration assay and a comet assay (up to 1 mg/ml). Laminaria Japonica Extract (up to 5000 µg/plate) was not mutagenic in an Ames assay and a chromosome aberration assay. Undaria Pinnatifida Extract was not genotoxic in Ames assays and chromosome aberration assays (up to 5000 µg/ml). In micronucleus assays, Ecklonia Cava Extract (up to 3000 mg/kg), Laminaria Japonica Extract (up to 2000 mg/kg), and Undaria Pinnatifida Extract (up to 2000 mg/kg) were not genotoxic.

None of the orally or dermally administered brown algae-derived ingredients tested (e.g., Hizikia Fusiforme Extract, Saccharina Angustata Extract (inference from *Saccharina angustata* powder), Undaria Pinnatifida Extract, and Undaria Pinnatifida Powder) were tumor (mammary and colorectal) promoters, but decreased the number, incidence, and/or size of tumors in rats. AOM or DMBA was used for initiation; TPA was used for promotion. Rats administered MNNG followed by 8 weeks of Sargassum Pallidum Extract (400 to 800 mg/kg/day) in drinking water exhibited decreased inflammatory responses.

A *Fucus vesiculosus* extract exhibited estrogen effects in several in vitro studies. This extract (50 and 75 µmol/l) reduced 17-β-estradiol levels in human granulosa cells and also competed with estradiol and progesterone for binding to their receptors. In another study, a *Fucus vesiculosus* extract competed for and bound to ERα (IC_{50} = 42.2 µmol/l), ERβ (IC_{50} = 31.8 µmol/l), and PR-B (IC_{50} = 31.8 µmol/l), with a slightly higher affinity for ERβ. In co-treatments with E2 (12.5 pM; EC_{50}), a *Fucus vesiculosus* extract (2%) reduced the activation of the luciferase reporter by up to 50%, exhibiting potent ER antagonistic effects. ER-dependent and -independent cancer cell lines showed significantly decreased viability with increasing test material concentrations. The cell line-specific sensitivity suggests that *Fucus vesiculosus* extract was not toxic at up to 2%, but instead induces cell death through modulated pathways. In one study, aromatase activity following treatment of hLGCs with a *Fucus vesiculosus* extract (10 to 100 µmol/L) did not change.

In in vivo studies, a *Fucus vesiculosus* powder exhibited estrogenic effects. Daily oral administration (175 and 350 mg/kg/day) for 4 weeks resulted in a dose-dependent increase in the length of the estrous cycle and an overall 100% increase in the mean length of the diestrus phase of the estrous cycle in the treated rats. Mean serum 17-β-estradiol levels were reduced at 2 weeks and further reduced at 4 weeks. Female rats that had naturally high circulating estradiol had reduced serum 17-β-estradiol (25% to 58% in all but 2 rats) after 1 week oral administration of a *Fucus vesiculosus* powder (350 mg/kg/day). This powder (700 and 1400 mg/day) increased the menstrual cycle length and reduced the days of menstruation in a dose-dependent manner in three female human subjects with hypermenorrhea, dysmenorrhea, and other related ailments. In one subject, the plasma estradiol levels were decreased and the progesterone levels were increased in a dose-dependent manner.

An *Ascophyllum nodosum* extract (0.5 g in water) administered to the shaved backs of rabbits under semi-occlusion for 4 h was not irritating. A skin cream containing a *Laminaria japonica* extract (10%; 20 mg) was not irritating to human subjects.

In a photo-protection study involving a *Sargassum muticum* extract, the effect of this extract against cell death induced by UVB radiation was studied. Cell viability was 61% in UVB (150 mJ/cm^2) irradiated cells and 70% in UVB-irradiated cells treated with SME. Decreased numbers of apoptotic bodies as well as DNA fragmentation was apparent in cells exposed to SME and UVB versus UVB exposure alone.

An *Ascophyllum nodosum* extract (100 mg) administered to the eyes of rabbits had a maximum irritation score was 6.7 out of 8 at 1 h post-instillation. The score decreased to 0 by day 7 and was rated as a mild ocular irritant.

In oral human clinical trials, adverse effects of *Ascophyllum nodosum* powder (0.5g/d), an *Ecklonia cava* extract (up to 400 mg/day), and an *Undaria pinnatifida* powder (average intake 3.3 g per day) were mild and transient. The adverse effects included nausea, indigestion, dyspepsia, and diarrhea.

A gel with an aqueous *Fucus vesiculosus* extract (1%; 0.2 ml) was applied to one cheek of human subjects at least twice per day (morning and evening) for 5 weeks. There were no signs of erythema or edema during the experiment.

DATA NEEDS

The CIR is seeking, at a minimum, the following information on brown algae-derived cosmetic ingredients for use in the resulting safety assessment:

1. Chemical characterization data of each ingredient as used in cosmetics
2. Dermal and inhalation toxicity data
3. Dermal irritation and sensitization data on brown algae-derived ingredients, at maximum use concentrations
4. Because these ingredients are botanicals and composition and extraction methods vary, specific chemical composition data, as well as the extraction solvent used for each cosmetic product being tested, should be included with all data that are submitted

TABLES

Table 1. Brown algae ingredients included in this assessment

Agarum Cribrosum Extract	Fucus Spiralis Extract Fucus Vesiculosus	Macrocystis Pyrifera (Kelp) Juice Macrocystis Pyrifera (Kelp) Protein
Alaria Esculenta Extract	Fucus Vesiculosus Extract	Nereocystis Luetkeana Extract
Ascophyllum Nodosum	Fucus Vesiculosus Powder	Pelvetia Canaliculata Extract
Ascophyllum Nodosum Extract	Halidrys Siliquosa Extract	Pelvetia Siliquosa Extract
Ascophyllum Nodosum Powder	Halopteris Scoparia Extract	Phyllacantha Fibrosa Extract
Asterionellopsis Glacialis Extract	Himanthalia Elongata Extract	Rissoella Verruculosa Extract
Cladosiphon Novae-Caledoniae Extract	Himanthalia Elongata Powder	Saccharina Angustata Extract
Cladosiphon Okamuranus Extract	Hizikia Fusiforme Extract	Saccharina Japonica Extract
Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract	Hizikia Fusiformis Water	Saccharina Longicruris Extract
	Hizikia Fusiformis Callus Culture Extract	Sargassum Filipendula Extract
Cystoseira Baccata Extract	Hydrolyzed Ecklonia Cava Extract	Sargassum Fulvellum Extract
Cystoseira Balearica Extract	Hydrolyzed Fucus Vesiculosus Extract	Sargassum Fusiforme Extract
Cystoseira Caespitosa Extract	Hydrolyzed Fucus Vesiculosus Protein	Sargassum Glaucescens Extract
Cystoseira Compressa Extract	Laminaria Cloustoni Extract	Sargassum Horneri Extract
Cystoseira Compressa Powder	Laminaria Diabolica Extract	Sargassum Muticum Extract
Cystoseira Tamariscifolia Extract	Laminaria Digitata Extract	Sargassum Pallidum Extract
Dictyopteris Polypodioides Extract	Laminaria Digitata Powder	Sargassum Siliquastrum Extract
Dictyota Coriacea Extract	Laminaria Hyperborea Extract	Sargassum Thunbergii Extract
Durvillaea Antarctica Extract	Laminaria Japonica Extract	Sargassum Vulgare Extract
Ecklonia Cava Extract	Laminaria Japonica Powder	Sahel Scenedesmus Extract
Ecklonia Cava Water	Laminaria Longissima Extract	Sphacelaria Scoparia Extract
Ecklonia Kurome Extract	Laminaria Ochroleuca Extract	Undaria Peterseniana Extract
Ecklonia Kurome Powder	Laminaria Saccharina Extract	Undaria Pinnatifida Extract
Ecklonia/Laminaria Extract	Lessonia Nigrescens Extract	Undaria Pinnatifida Cell Culture Extract
Ecklonia Maxima Extract	Lessonia Nigrescens Powder	Undaria Pinnatifida Leaf/Stem Extract
Ecklonia Maxima Powder	Macrocystis Pyrifera (Kelp)	Undaria Pinnatifida Powder
Ecklonia Radiata Extract	Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	Undaria Pinnatifida Root Powder
Eisenia Arborea Extract		
Fucus Serratus Extract	Macrocystis Pyrifera (Kelp) Extract	

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

Ingredient	Definition	Function
Agarum Cribrosum Extract	Agarum Cribrosum Extract is the extract of the alga, *Agarum cribrosum.*	Skin-conditioning agent - miscellaneous
Alaria Esculenta Extract	Alaria Esculenta Extract is the extract of the alga, *Alaria esculenta.*	Hair conditioning agent; skin protectant
Ascophyllum Nodosum	Ascophyllum Nodosum is the alga, *Ascophyllum nodosum.*	Skin-conditioning agent - miscellaneous
Ascophyllum Nodosum Extract 84775-78-0	Ascophyllum Nodosum Extract is the extract of the alga, *Ascophyllum nodosum.*	Skin-conditioning agent - miscellaneous
Ascophyllum Nodosum Powder	Ascophyllum Nodosum Powder is the powder obtained from the dried, ground alga, *Ascophyllum nodosum.*	Skin-conditioning agent - miscellaneous
Asterionellopsis Glacialis Extract	Asterionellopsis Glacialis Extract is the extract of the alga, *Asterionellopsis glacialis.*	Antioxidant; skin-conditioning agent – miscellaneous; pH adjuster
Cladosiphon Novae-Caledoniae Extract	Cladosiphon Novae-Caledoniae Extract is the extract of the alga, *Cladosiphon novae-caledoniae.*	Humectant; skin protectant
Cladosiphon Okamuranus Extract	Cladosiphon Okamuranus Extract is the extract of the alga, *Cladosiphon okamuranus.*	Skin-conditioning agent - miscellaneous
Cystoseira Amentacea/Caespitosa/ Branchycarpa Extract	Cystoseira Amentacea/Caespitosa/Branchycarpa Extract is the extract of the algae, *Cystoseira amentacea, Cystoseira caespitosa*, and *Cystoseira branchycarpa.*	Skin-conditioning agent - miscellaneous
Cystoseira Baccata Extract	Cystoseira Baccata Extract is the extract of the alga, *Cystoseira baccata.*	Skin-conditioning agent - miscellaneous
Cystoseira Balearica Extract	Cystoseira Balearica Extract is the extract of the alga, *Cystoseira balearica.* The accepted scientific name for *Cystoseira balearica* is *Cystoseira brachycarpa.*	Skin-conditioning agent - miscellaneous
Cystoseira Caespitosa Extract	Cystoseira Caespitosa Extract is the extract of the alga, *Cystoseira caespitosa.* The accepted scientific name for *Cystoseira caespitosa* is *Cystoseira brachycarpa*.	Skin protectant
Cystoseira Compressa Extract	Cystoseira Compressa Extract is the extract of the alga, *Cystoseira compressa.*	Skin-conditioning agent - miscellaneous
Cystoseira Compressa Powder	Cystoseira Compressa Powder is the dried, ground powder obtained from the alga, *Cystoseira compressa.*	Skin-conditioning agent - miscellaneous
Cystoseira Tamariscifolia Extract	Cystoseira Tamariscifolia Extract is the extract of the alga, *Cystoseira tamarisfolia.*	Skin-conditioning agent - miscellaneous

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

Ingredient	Definition	Function
Dictyopteris Polypodioides Extract	Dictyopteris Polypodioides Extract is the extract of the alga, *Dictyopteris polypodioides.*	Skin-conditioning agent – emollient; skin-conditioning agent - miscellaneous
Dictyopteris Membranacea Extract (Retired)	Dictyopteris Membranacea Extract (Retired) is the extract of the alga, *Dictyopteris membranacea*. The INCI Name, Dictyopteris Membranacea Extract, originally published in 2007, was designated with a retired status in 2015. For an interim period of time, trade name assignments formerly published with the INCI Name Dictyopteris Membranacea Extract will be retained in the retired monograph, and also published with the new name assignment based on the current genus and species name, Dictyopteris Polypodioides Extract.	Antioxidant
Dictyota Coriacea Extract	Dictyota Coriacea Extract is the extract of the alga, *Dictyota coriacea*.	Oxidizing agent
Durvillaea Antarctica Extract	Durvillaea Antarctica Extract is the extract of the alga, *Durvillaea antarctica.*	Skin-conditioning agent - miscellaneous
Ecklonia Cava Extract	Ecklonia Cava Extract is the extract of the alga, *Ecklonia cava.*	Humectant; skin-conditioning agent - humectant
Ecklonia Cava Water	Ecklonia Cava Water is the aqueous solution of the steam distillates obtained from the whole ~~plant~~, *Ecklonia cava*.	Skin protectant
Ecklonia Kurome Extract	Ecklonia Kurome Extract is the extract of the alga, *Ecklonia kurome.*	Skin-conditioning agent – humectant; skin-conditioning agent - miscellaneous
Ecklonia Kurome Powder	Ecklonia Kurome Powder is the powder obtained from the dried, ground alga, *Ecklonia kurome*.	Skin-conditioning agent - humectant
Ecklonia/Laminaria Extract	Ecklonia/Laminaria Extract is the extract of a mixture of the algae, *Ecklonia* and *Laminaria.*	Skin-conditioning agent - miscellaneous
Ecklonia Maxima Extract	Ecklonia Maxima Extract is the extract of the alga, *Ecklonia maxima*.	Skin-conditioning agent - miscellaneous
Ecklonia Maxima Powder	Ecklonia Maxima Powder is the powder obtained from the dried, ground alga, *Ecklonia maxima*.	Skin-conditioning agent - miscellaneous
Ecklonia Radiata Extract	Ecklonia Radiata Extract is the extract of the alga, *Ecklonia radiata.*	Hair conditioning agent; skin-conditioning agent - miscellaneous
Eisenia Arborea Extract	Eisenia Arborea Extract is the extract of the alga, *Eisenia arborea*.	Skin-conditioning agent - miscellaneous
Fucus Serratus Extract 94167-02-9	Fucus Serratus Extract is the extract of the alga, *Fucus serratus.*	Skin-conditioning agent - miscellaneous
Fucus Spiralis Extract	Fucus Spiralis Extract is the extract of the alga, *Fucus spiralis.*	Skin-conditioning agent – emollient; skin-conditioning agent - miscellaneous
Fucus Vesiculosus	Fucus Vesiculosus is the alga, *Fucus vesiculosus.*	Skin-conditioning agent - miscellaneous
Fucus Vesiculosus Extract 283-633-7	Fucus Vesiculosus Extract is the extract of the alga, *Fucus vesiculosus.*	Fragrance ingredient; skin-conditioning agent - miscellaneous
Fucus Vesiculosus Powder	Fucus Vesiculosus Powder is the powder obtained from dried, ground *Fucus vesiculosus.*	Skin-conditioning agent - miscellaneous
Halidrys Siliquosa Extract	Halidrys Siliquosa Extract is the extract of the alga, *Halidrys siliquosa*.	Skin-conditioning agent - miscellaneous
Halopteris Scoparia Extract	Halopteris Scoparia Extract is the extract of the alga, *Halopteris scoparia*.	Skin-conditioning agent - miscellaneous
Himanthalia Elongata Extract	Himanthalia Elongata Extract is the extract of the thallus of the alga, *Himanthalia elongata.*	Skin-conditioning agent - miscellaneous
Himanthalia Elongata Powder	Himanthalia Elongata Powder is the powder obtained from the dried, ground alga, *Himanthalia elongata*.	Absorbent; binder; viscosity increasing agent -aqueous
Hizikia Fusiforme Extract	Hizikia Fusiforme Extract is the extract of the alga, *Hizikia fusiforme.* The accepted scientific name for *Hizikia fusiforme* is *Sargassum fusiforme.*	Skin protectant; skin-conditioning agent - miscellaneous
Hizikia Fusiformis Water	Hizikia Fusiformis Water is the aqueous solution of the steam distillates obtained from the alga, *Hizikia fusiformis.*	Skin protectant
Hizikia Fusiformis Callus Culture Extract	Hizikia Fusiformis Callus Culture Extract is the extract of a culture of the callus of *Hizikia fusiformis*. The accepted scientific name for *Hizikia fusiformis* is *Sargassum fusiforme.*	Antifungal agent; antioxidant; hair conditioning agent; skin-conditioning agent - miscellaneous
Hydrolyzed Ecklonia Cava Extract	Hydrolyzed Ecklonia Cava Extract is the hydrolysate of an extract of the alga, *Ecklonia cava* derived by acid, enzyme or other method of hydrolysis.	Skin-conditioning agent - miscellaneous
Hydrolyzed Fucus Vesiculosus Extract 84696-13-9	Fucus Vesiculosus Extract is the extract of the alga, *Fucus vesiculosus.*	Fragrance ingredient; skin-conditioning agent – miscellaneous
Hydrolyzed Fucus Vesiculosus Protein	Hydrolyzed Fucus Vesiculosus Extract is the extract of the hydrolysate of *Fucus vesiculosus* derived by acid, enzyme or other method of hydrolysis.	None reported
Laminaria Cloustoni Extract 90046-11-0 92128-82-0	Laminaria Cloustoni Extract is the extract of the alga, *Laminaria cloustoni.* The accepted scientific name for *Laminaria cloustoni* is *Laminaria hyperborea.*	Fragrance ingredient
Laminaria Diabolica Extract	Laminaria Diabolica Extract is the extract of the alga, *Laminaria diabolica*. The accepted scientific name for *Laminaria diabolica* is *Saccharina japonica.*	Skin-conditioning agent - humectant

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

Ingredient	Definition	Function
Laminaria Digitata Extract 90046-12-1 92128-82-0	Laminaria Digitata Extract is the extract of the alga, *Laminaria digitata.*	Fragrance ingredient; skin protectant; skin-conditioning agent - miscellaneous
Laminaria Digitata Powder	Laminaria Digitata Powder is the powder obtained from the dried, ground thallus of the alga, *Laminaria digitata.*	Skin-conditioning agent - miscellaneous
Laminaria Hyperborea Extract 90046-13-2 92128-82-0	Laminaria Hyperborea Extract is the extract of the alga, *Laminaria hyperborea*.	Fragrance ingredient; skin protectant
Laminaria Japonica Extract 92128-82-0	Laminaria Japonica Extract is the extract of the alga, *Laminaria japonica.* The accepted scientific name for *Laminaria japonica* is *Saccharina japonica*.	Fragrance ingredient
Laminaria Japonica Powder	Laminaria Japonica Powder is the powder obtained from the dried, ground alga, *Laminaria japonica.* The accepted scientific name for *Laminaria japonica* is *Saccharina japonica.*	Skin-conditioning agent - miscellaneous
Laminaria Longissima Extract	Laminaria Longissima Extract is the extract of the alga, *Laminaria longissima.* The accepted scientific name for *Laminaria longissima* is *Saccharina longissima*	Skin-conditioning agent - humectant
Laminaria Ochroleuca Extract 92128-82-0	Laminaria Ochroleuca Extract is the extract of the alga, *Laminaria ochroleuca*. The accepted scientific name for *Laminaria ochroleuca* is *Saccharina japonica.*	Fragrance ingredient; skin-conditioning agent - miscellaneous
Laminaria Saccharina Extract 90046-14-3 92128-82-0	Laminaria Saccharina Extract is the extract of the thallus of the alga, *Laminaria saccharina.* The accepted scientific name for *Laminaria saccharina* is *Saccharina latissima.*	Fragrance ingredient; skin-conditioning agent - miscellaneous
Lessonia Nigrescens Extract	Lessonia Nigrescens Extract is the extract of the alga, *Lessonia nigrescens.*	Skin protectant
Lessonia Nigrescens Powder	Lessonia Nigrescens Powder is the powder obtained from the dried, ground alga, *Lessonia nigrescens.*	Binder
Macrocystis Pyrifera (Kelp)	Macrocystis Pyrifera (Kelp) is the alga, *Macrocystis pyriferae*.	Viscosity increasing agent - aqueous
Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract	Macrocystis Pyrifera (Kelp) Blade/Pneumatocyst/Stipe Juice Extract is the extract of the juice derived from the blade, pneumatocyst and stipe of the alga, *Macrocystis pyrifera.*	Skin-conditioning agent - miscellaneous
Macrocystis Pyrifera (Kelp) Extract 347174-92-9	Macrocystis Pyrifera (Kelp) Extract is the extract of the alga, *Macrocystis pyrifera.*	Skin-conditioning agent - miscellaneous
Macrocystis Pyrifera (Kelp) Juice	Macrocystis Pyrifera (Kelp) Juice is the juice expressed from the alga, *Macrocystis pyrifera*.	Skin-conditioning agent - miscellaneous
Macrocystis Pyrifera (Kelp) Protein	Macrocystis Pyrifera (Kelp) Protein is the protein derived from the alga, *Macrocystis pyrifera*.	Skin-conditioning agent - miscellaneous
Nereocystis Luetkeana Extract	Nereocystis Luetkeana Extract is the extract of the alga, *Nereocystis luetkeana*.	Hair conditioning agent; skin-conditioning agent - miscellaneous
Pelvetia Canaliculata Extract 223751-75-5	Pelvetia Canaliculata Extract is the extract of the alga, *Pelvetia canaliculata.*	Skin protectant; skin-conditioning agent - miscellaneous
Pelvetia Siliquosa Extract	Pelvetia Siliquosa Extract is the extract of the alga, *Pelvetia siliquosa.*	Antioxidant; skin protectant; skin-conditioning agent - humectant
Phyllacantha Fibrosa Extract	Phyllacantha Fibrosa Extract is the extract of the alga, *Phyllacantha fibrosa.* The accepted scientific name for *Phyllacantha fibrosa* is *Cystoseira baccata.*	Skin-conditioning agent - miscellaneous
Rissoella Verruculosa Extract	Rissoella Verruculosa Extract is the extract of the alga, *Rissoella verruculosa.*	Skin protectant
Saccharina Angustata Extract	Saccharina Angustata Extract is the extract of the alga, *Saccharina angustata*.	Skin-conditioning agent - emollient; skin-conditioning agent - miscellaneous
Laminaria Angustata Extract (Retired)	Laminaria Angustata Extract (Retired) is the extract of the alga, *Laminaria angustata*. The INCI Name, Laminaria Angustata Extract, originally published in 2003, was designated with a retired status in 2015. For an interim period of time, trade name assignments formerly published with the INCI Name Laminaria Angustata Extract will be retained in the retired monograph, and also published with the new name assignment based on the current genus and species name, Saccharina Angustata Extract.	Skin-conditioning agent - miscellaneous
Saccharina Japonica Extract	Saccharina Japonica Extract is the extract of the alga, *Saccharina japonica*.	Skin-conditioning agent - miscellaneous
Laminaria Ochotensis Extract (Retired)	Laminaria Ochotensis Extract (Retired) is the extract of the alga, *Laminaria ochotensis.* The INCI Name, Laminaria Ochotensis Extract, originally published in 2008, was designated with a retired status in 2015. For an interim period of time, trade name assignments formerly published with the INCI Name Laminaria Ochotensis Extract will be retained in the retired monograph, and also published with the new name assignment based on the current genus and species name, Saccharina Japonica Extract.	Skin-conditioning agent - emollient
Saccharina Longicruris Extract	Saccharina Longicruris Extract is the extract of the alga, *Saccharina longicruris.*	Skin-conditioning agent - humectant
Sargassum Filipendula Extract	Sargassum Filipendula Extract is the extract of the brown alga, *Sargassum filipendula.*	Skin-conditioning agent - miscellaneous

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

Ingredient	Definition	Function
Sargassum Fulvellum Extract	Sargassum Fulvellum Extract is the extract of the alga, *Sargassum fulvellum.*	Skin-conditioning agent - miscellaneous
Sargassum Fusiforme Extract	Sargassum Fusiforme Extract is the extract of the brown alga, *Sargassum fusiforme.*	Skin-conditioning agent - miscellaneous
Sargassum Glaucescens Extract	Sargassum Glaucescens Extract is the extract of the alga, *Sargassum glaucescens.*	Antioxidant
Sargassum Horneri Extract	Sargassum Horneri Extract is the extract of the alga, *Sargassum horneri.*	Skin-conditioning agent - miscellaneous
Sargassum Muticum Extract	Sargassum Muticum Extract is the extract of the alga *Sargassum muticum.*	Skin-conditioning agent - miscellaneous
Sargassum Pallidum Extract	Sargassum Pallidum Extract is the extract of the alga, *Sargassum pallidum.*	Antifungal agent; antioxidant
Sargassum Siliquastrum Extract	Sargassum Siliquastrum Extract is the extract of the alga, *Sargassum siliquastrum.*	Skin-conditioning agent - miscellaneous
Sargassum Thunbergii Extract	Sargassum Thunbergii Extract is the extract of the alga, *Sargassum thunbergii.*	Antimicrobial agent
Sargassum Vulgare Extract	Sargassum Vulgare Extract is the extract of the alga, *Sargassum vulgare.*	Skin-conditioning agent - miscellaneous
Sahel Scenedesmus Extract	Sahel Scenedesmus Extract is the extract of the alga, *Scenedesmus.*	Skin protectant
Sphacelaria Scoparia Extract	Sphacelaria Scoparia Extract is the extract of the alga, *Sphacelaria scoparia.* The accepted scientific name for *Sphacelaria scoparia* is *Halopteris scoparia.*	Corn/callus/wart remover
Undaria Peterseniana Extract	Undaria Peterseniana Extract is the extract of the alga *Undaria peterseniana.*	Skin-conditioning agent - miscellaneous
Undaria Pinnatifida Extract	Undaria Pinnatifida Extract is the extract of the alga, *Undaria pinnatifida.*	Skin protectant; skin-conditioning agent - miscellaneous
Undaria Pinnatifida Cell Culture Extract	Undaria Pinnatifida Cell Culture Extract is the extract of a cell culture suspension of *Undaria pinnatifida.*	Hair conditioning agent; skin-conditioning agent - miscellaneous
Undaria Pinnatifida Leaf/Stem Extract	Undaria Pinnatifida Leaf/Stem Extract is the extract of the leaves and stems of *Undaria pinnatifida.*	Skin-conditioning agent – emollient
Undaria Pinnatifida Powder	Undaria Pinnatifida Powder is the powder obtained from the dried, ground alga, *Undaria pinnatifida.*	Absorbent; binder; viscosity increasing agent - nonaqueous
Undaria Pinnatifida Root Powder	Undaria Pinnatifida Root Powder is the powder obtained from the dried, ground root-like structures of the alga, *Undaria pinnatifida.*	Humectant; skin-conditioning agent - humectant

Table 3. **Descriptions of the major groups of algae**

Common Name	Phylum	Kingdom	Description	Reference
Brown Algae	Phaeophyta	Stramenopila	-mostly large, leathery seaweeds -cellulose wall with alginic acid and fucoidan -derived alginic acid is used as a suspending, emulsifying, gel-forming and film-forming agent	[12]
Green Algae	Chlorophyta	Plantae	-usually green in color -cellulose cell walls -store starch -beta carotene -chlorophyll a & b	[12]
Diatoms	Bacillariophyta	Stramenopila	-golden brown in color -silica cell walls -store oil as food reserve -carotenoids -chlorophyll a & c	[12]
Chrysophytes	Chrysophyta	Stramenopila	-consists of diatoms, golden-brown algae and yellow-green algae -cellulose cell walls with large amounts of silica -chlorophyll a &c	[12,81]
Blue Green Algae	Cyanophyta	Monera	-phycobilins present -store glycogen -prokaryotic -chlorophyll a -some are toxic	[12]

Table 3. **Descriptions of the major groups of algae**

Common Name	Phylum	Kingdom	Description	Reference
Red Algae	Rhodophyta	Rhodophyta	-phycobilins present -store floridean starch -cellulose cell wall -chlorophyll a & d -source of agar -used as a stabilizer and thickener in many products	[12]
Dinoflagellates	Pyrrhophyta	Alveolata	-some produce toxins -mostly marine	[12,82]
Euglenoids	Euglenophyta	Euglenozoa	-common in freshwater -can be parasitic	[12,83]

Table 4.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Agarum cribrosum	-	North Atlantic (Massachusetts to east Greenland) and North Pacific (Washington state to Japan and Russia) Forms thick beds at depths of 10-12 m	[84]
Alaria esculenta (dabberlocks, badderlocks, winged kelp)	Plants with olive or yellow-brown fronds to 4 m long and 25 cm wide, more often about 1 m and 7.5 cm wide. Attached by a root-like holdfast at the base from which a narrow flexible stipe arises which continues into the leafy part of the plant as a distinct mid-rib, generally with a yellow-brown color. The reproductive structures, apparent as dark-brown areas, are confined to unbranched leafy appendages borne on the stipe, usually in two rows.	North Atlantic Ocean Generally growing on rock in wave-exposed places, often forming a band at low water and in the shallow subtidal, but also occurring in tidal pools in the lower shore.	[84,85]
Ascophyllum nodosum (asco, sea whistle, bladderwrack, rockweed)	Closely related to *Fucus*. Up to 3 m in height and is yellow in areas exposed to sunlight and dark green or brown in its shaded parts. Single bladders are central in long, strap-like fronds. Fronds hang downwards. Multiple fronds grow from each basal holdfast, and the plant generally regenerates new fronds from base when one of the larger fronds is damaged. Reproduction takes place in spring in yellow receptacles, which develop in response to short days in autumn, mature during winter, and are at their most prolific in spring. Eggs and sperm are released into water, and eggs release a low molecular weight pheromone, finnavarene.	North Atlantic basin (Virginia to Spain) Has been observed in San Francisco Bay, but does not persist there. Sheltered intertidal rocks in shallow (usually where it is exposed at low or extreme low tides)	[84-87]
Cystoseira baccata (bushy berry wrack)	Thallus to 1 m long, usually solitary, attached by a thick, conical attachment disc. Axis simple or branched, and flattened; apex smooth and surrounded during periods of active growth by incurved young laterals. Lateral branch systems alternate, radially symmetrical, profusely branched in a repeatedly pinnate fashion and bearing sparse, filiform, occasionally bifurcated appendages on the branches; deciduous, leaving decurrent bases which give an irregular, zigzag outline to the axis. Air vesicles present in axes of branches of higher order, sometimes in chains; seasonal, particularly numerous in autumn. Receptacles 1-5 cm long, formed from axes of ultimate ramuli, irregularly nodose and bearing simple, filiform appendages.	S England, W Ireland north to W Scotland. Has been noted down to Morocco and in Mediterranean Sea. Lower intertidal in large sandy pools or lagoons, mostly in persistent stands.	[84,85]
Cystoseira tamariscifolia (bushy rainbow wrack)	Solitary thalli, up to 1 m long, bushy, with a pronounced greenish or bluish iridescence when submerged or wet; attached by a conical disc. Axis is cylindrical, up to 60 cm long, usually branched and with an inconspicuous apex. Lateral branch systems arising in spiral sequence, up to 60 cm long, profusely branched in a repeatedly pinnate fashion, showing radial symmetry with simple or bifid spine-like appendages: deciduous, leaving prominent scars or stumps. Cryptostomata present on branches and appendages. Ovoid air vesicles often present in axes of ultimate ramuli. Receptacles 1-2 cm long, formed from terminal regions of ultimate ramuli.	Western Mediterranean Sea/northern Africa to Ireland Large intertidal rock pools and lagoons and shallow subtidal shores	[84,85]
Dictyopteris polypodioides [*Dictyopteris membranacea* (Retired)]	Thallus flat and leaf-like, to 300 mm long and 20-30 mm broad; fronds olive to yellow-brown, translucent, and somewhat regularly dichotomously forked with a prominent midrib extending to the apices. Margins sometimes split to midrib. Has an unpleasant smell shortly after collection, which degenerates quickly.	Ireland (except for east coast), west Scotland, Wales, southwest England, to Portugal and West Africa Large pools at low water and shallow subtidal shores	[84,85]

Table 4.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Fucus serratus (serrated wrack, saw wrack, toothed wrack)	Dichotomously branched fronds arising from a small disc via a short stipe; distinct midrib. Plants grow to 300 mm with terminal, compressed receptacles with warty conceptacles. It is easily recognized by its saw-toothed frond, and a lack of swollen receptacles.	Widely distributed on all coasts of Britain and Ireland. Baltic Sea to Spain and Canary Islands. Introduced to Nova Scotia and has spread to New Brunswick and Maine. Zone forming on sheltered and semi-exposed shores.	84-86
Fucus spiralis (jelly bags, spiral wrack, flat wrack spiraled wrack)	Fronds lack bladders; elongated air bladders are on either side of the midrib. Fronds have twisted, dichotomous branches. Plant is up to 20 cm long, attached to the substratum with a discoid holdfast. Color ranges from dark brown to olive-green.	North Atlantic and North Pacific; Baltic Sea to Morocco/Canary Islands and New York; Alaska to California. Introduced to Mediterranean Sea (France). Uppermost species of *Fucus* that occurs on shore.	86
Fucus vesiculosus (paddy tang, red fucus, dyers fucus, swine tang, sea ware, bladder, rockweed, bladderwrack, popping wrack, wrack)	Paired bladders occur on either side of a prominent midrib. Frond is generally not strongly spiraled and receptacles do not have a sterile rim, and frond does not have a serrated margin. Attached by a small, strong disc which gives rise to a short stipe. Plant is 15 to 90 cm long and 0.6 to 2.5 cm wide. Reproductive receptacles are swollen areas at tips of fronds that have many flask-shaped cavities called conceptacles, which house male and female reproductive structures known as antheridia (borne on antheridiophores) and oogonia (containing 8 eggs), respectively. Eggs and sperm are liberated onto surface of receptacles and a pheromone (sex-attracting substance) is released by eggs that attract sperm. Fertilization results in a zygote that forms a new *Fucus* adult.	North Atlantic (Canadian Arctic, Russia, White Sea, Baltic Sea) south to Canary Islands and West Indies Midshore zone A bladderless form occurs on more wave-exposed shores in the NE Atlantic. Grows in various conditions, from saline lagoons to exposed rocky shores, as well as on sheltered rocky shores. Forms dense canopies.	84-86,88
Halidrys siliquosa (podweed, sea oak)	Thallus 30-130 cm long, tawny to yellow-brown ochre, tough and leathery; attached by a large, discoid holdfast, giving rise to compressed, irregularly alternately branched fronds, with several orders of close branching in the same plane. Pod-shaped, segmented air bladders are produced replacing some lateral branches. Reproductive conceptacles forming in swollen conceptacles at apices of branches	Northeast Atlantic (Norway/Baltic Sea to Morocco) Large, mid-intertidal pools, often dominating in very large, sunny pools, but more often forming occasional stands. Occasionally forming extensive forests in shallow subtidal to about 10 m, generally in current-exposed locations. Widespread and common. Halidrys produces meroditerpenoids that seemingly act as antifouling agents preventing other organisms adhering to surface of the plant.	84,85
Halopteris scoparia (sea flax weed)	*Stypocaulon scoparium* may be synonymous	Northwest Atlantic (Baltic Sea to Canary Islands) and Mediterranean Sea	84
Himanthalia elongata (thongweed, buttonweed, sea spaghetti, sea thong, sea haricots)	Long thong-like fronds, basal mushroom-like buttons. Thallus consisting of a button-shaped vegetative thallus to 30 mm wide and 25 mm high, and a long, narrow, strap-like, sparingly branched, light yellow-brown reproductive receptacle to 2 m in length and up to 10 mm in width, on which conceptacles are borne. Buttons, initially club-shaped but later mushroom-like, develop from zygotes in late summer, mature in winter, and begin to form reproductive receptacles in January/February. Some 4-6 dichotomies are produced at this stage, and fronds then elongate and thicken, developing no further branches, and become reproductively mature in July-September.	Northwest Atlantic Ocean (Scandinavia to Spain) Gently sloping rocks, particularly on semi-wave-exposed shore, on which they may form a distinct zone at low water. Sparse populations sometimes develop in sheltered lagoons where the plants are more yellow and less flattened.	84,85

Table 4.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Laminaria cloustoni [*Laminaria hyperborea*] (kelp, may weed, kelpie, liver weed, mirkle, pennant weed, strapwrack, cuvie, tangle, split whip wrack, sea rods, forest kelp, northern kelp)	Dark brown, to 2 m in length; with a claw-like, conical holdfast, a rough, rigid stipe which generally rises up out of the water, and is covered in epiphytes when older, and a laminate blade to 1.5 m long dividing into finger-like segments. Stipe is rugose (rough) when older, circular in cross-section, and snaps easily when bent; the holdfast is conical.	Northwest Atlantic Ocean (Scandinavia to Spain) Common at extreme low water in wave-exposed areas, and in the subtidal in optically clear water growing on rock to a depth of 32 m. Forms extensive closed communities at depths of 0-24 m. There are usually large quantities of ephytic red algae growing on the older stipes; the old fronds are cast off in spring and new ones grow below for a time.	84,85
Laminaria digitata (kelp)	Dark brown, to 2 m in length; with a claw-like holdfast, a smooth, flexible stipe, and a laminate blade to 1.5 m long split into finger-like segments. The stipe is oval in cross-section, and does not snap easily when bent. Underwater plants are more golden in color in sunlight.	North Atlantic (Arctic Canada/ Baltic Sea/Russia to Spain and New England) Very common in lower intertidal and shallow subtidal growing on rock. May form extensive meadows at low tide.	84,85
Laminaria hyperborea (kelpie, liver weed, mirkle, pennant weed, strapwrack, cuvie, tangle, split whip wrack)	Dark brown, to 2 m in length; with a claw-like, conical holdfast, a rough, rigid stipe which generally sticks up out of the water, and is covered in epiphytes when older, and a laminate blade to 1.5 m long dividing into finger-like segments. Stipe is rugose (rough) when older, circular in cross-section, and snaps easily when bent; the holdfast is conical.	Northeast Atlantic (Scandinavia/Iceland to Spain and Canary Islands) Common at extreme low water in wave-exposed areas, and in subtidal in optically clear water growing on rock to a depth of 32 m. Forms extensive closed communities at depths of 0-24 m; there are usually large quantities of ephytic red algae growing on the older stipes; the old fronds are cast off in spring and new ones grow below for a time.	84,85,89
Laminaria saccharina [The accepted scientific name is *Saccharina latissima*] (sea belt, poor man's weather glass, sweet wrack, sugar wrack, sugar tang, oarweed, tangle, kelp, sugar sea belt, sweet tangle, sugarwrack, zuckertang)	Yellow brown, to 3 m in length; with a claw-like holdfast, a small, smooth, flexible stipe, and an undivided laminate blade to 3 m long with parallel, ruffled sides and a elongated, tongue-like appearance. Frond is characteristically dimpled with regular bullations (depressions). Stipe is relatively small, cylindrical in section and more flexible than those of *Laminaria digitata* and *Laminaria hyperborea*. It is only species in the NE Atlantic Ocean with an undivided frond, distinct bullations, and a frilly margin.	Circumboreal (Atlantic Ocean: Canada, Scandinavia, Greenland, Iceland to Galicia, Spain and Maine, but not known in the Bay of Biscay; Pacific Ocean: Alaska to California, Japan, Korea, Central Polynesia, India, New Zealand) Intertidal pools and occasional in shallow subtidal areas, becoming more abundant at low water in sheltered localities with fast-moving water, such as rapids systems. In subtidal, it is characteristic of intermittently disturbed areas.	84,85
Macrocystis pyrifera (giant kelp, sea ivy, giant pacific kelp)	Plants reach 45 meters long and grow in waters 6-20 (possibly up to 80) m deep, and grow at up to 30 cm per day. Now believed to be a monospecific genera ranging from intertidal to deep water with environments dictating morphology.	Eastern and southern Pacific Ocean in both hemispheres (Alaska to New Zealand and Australia) Dominant canopy-forming algae in southern and central California.	84,90,91
Pelvetia canaliculata (channeled wrack, cow tang)	Plants 80-120 mm long, yellow-brown in color, turning black when dry, and often so dry that fronds disintegrate when trodden upon; regularly dichotomously branched with a distinct channel on underside (side nearest rock), which holds moisture and apparently helps algae survive at very high levels on shore. Reproduction in conceptacles visible as dots on warty terminal receptacles. Usually infected by a fungus which may assist in allowing it to survive high in intertidal zone.	NE Atlantic from the Faroe Islands to Portugal Occurring very high on shore, generally above mean high water neap tides, on wave-exposed and sheltered shores, but absent from very exposed rocky shores.	84-86

Table 4.General characteristics and geographic distribution of brown algae species

Species (common name)	Description	Distribution/Habitat/Ecology	References
Sargassum muticum	Thallus bushy, elongated, yellowish-tawny to dark brown, generally to 4 m long (plants to 16 m have been reported from Brittany, but this is exceptional); tough, cylindrical, repeatedly alternately pinnately branched to the third or fourth order; whorls of distinctly flattened sculpted leaves at the base (resembling the leaves of Holly); with characteristic rounded-elliptical air bladders above and below, formed terminally. Reproductive receptacles below, formed in the axils of spiny leaves; spectacularly fecund. Basal holdfast penetrating and conical, persisting for several years. Reproductive plants detach easily, and continue to reproduce while drifting, and spreading the reproductive zygotes that develop on the surfaces of the receptacles. Terminal air bladders below; receptacles in the axils of spiny leaves.	Native to Japan; spread to China and Korea. Invasive in France, Spain and Portugal; western Mediterranean; Alaska south to Mexico. Throughout the intertidal in pools, but largest and commonest at low water.	[84,85]
Undaria pinnatifida (sea mustard, precious sea grass, wakame)	Thallus laminate, yellowish to dark brown, usually 1-2 m, occasionally 3 m or more in length; holdfast spreading, dichotomously branched and claw-like, giving rise to a flattened oar-like stipe with a "fried-egg" like margin with small proliferations and basally with beautifully lobed sporophylls that coil around it when mature; stipe continuing into the fond as a flattened midrib that bears broadly lobed laciniate fronds with a roughly pyramidal shape. Frilly sporophylls coiling around the base of the flattened stipe at the base. A similar flattened midrib is not found in any other kelp in the Atlantic. *Alaria esculenta* has a midrib which is not flattened and the frond of *Alaria* is not lobed, although it may be similarly laciniate.	Native to Pacific Russia, Japan, China and Korea. NE Ireland, S England, NW France, NW Spain, Mediterranean Lower intertidal and very shallow subtidal (no more than a few m), particularly in sheltered locations, growing particularly on marinas, buoys, and similar floating structures in harbors. Often occurring on boat-hulls.	[84]

Table 5. Chemical and physical properties of brown algae-derived ingredients.

Property	Value	Reference
Ascophyllum Nodosum Extract		
Physical Form	Liquid	92,93
	Viscous liquid	94
	Solid flakes	6
Color	Black	6,92
	Dark brown	93
	Dark brown (aq. ext)	94
Odor	Marine-like/Fish-like	92,93
	Characteristic, seaweed (aq. ext)	94
	Odorless	6
Density/Specific Gravity	1.17	92
	1.1 (aq. ext.)	94
Bulk Density (g/ml)	0.58	6
Viscosity kg/(s m)	< 0.1	92
Melting Point ^{o}C	0 (aq. ext.)	94
	> 300	6
Boiling Point ^{o}C	100	92
	100 (aq. ext.)	94
	65 – 96	93
Water Solubility g/L @ 20 ^{o}C & pH 7.4 – 7.5	> 10,000	6
@ 20 ^{o}C	100%	92,93
	100%	94
Other Solubility g/L		
Acetone @ 22 ^{o}C	0.007	6
Ethyl acetate @ 22^{o}C	0.009	6
Methanol @ 22 ^{o}C	0.251	6
log P_{ow}	-3.3 est.	5,6
Particle size	> 0.250 mm, 93.5%	6
	< 0.045 mm, none	
Ascophyllum Nodosum Powder		
Physical Form	Flakes or powder	95
	Powder	96
Color	Olive green	95
	Green	96
Odor	Marine-like	95
	Characteristic, fish-like	96
Water Solubility g/L	Insoluble	95
Ecklonia Cava Extract		
Physical Form	Powder (alcohol ext)	9
Color	Brown (alcohol ext)	9

aq. = aqueous; ext. = extract

Table 6. **Methods of manufacture for brown algae-derived ingredients.**

Ingredient (characterization)	Method of Manufacture	Reference
Cladosiphon Okamuranus Extract (high in fucoidan)	*Cladosiphon okamuranus* is hydrolyzed in 0.05 M or 0.5 M hydrochloric acid at 80°C for 30 min and then is neutralized with sodium hydroxide. Salt is removed by electrodialysis and then hydrolysate is lyophilized.	[19]
Dictyopteris Polypodioides Extract (high fractions of C_{11} hydrocarbons and sulfur compounds)	Air-dried plant material is extracted with diethyl ether. Solvent is removed vacuum distillation leaving a crude concrete extract. Crude extract is treated with hydrodistillation followed by liquid-liquid extraction with diethyl ether to obtain the essential oil.	[20]
Dictyopteris Polypodioides Extract (high fraction of sulfur compounds)	Air-dried plant material is extracted with diethyl ether. Solvent is removed by vacuum distillation leaving a crude concrete extract. Crude extract is then subjected to supercritical fluid (CO_2) extraction.	[20]
Dictyopteris Polypodioides Extract (high fractions of sesquiterpenes)	Air-dried plant material is extracted with diethyl ether. Solvent is removed vacuum distillation leaving a crude concrete extract. Crude extract is mixed with water and irradiated in a microwave oven (focused microwave-assisted hydrodistillation).	[20]
Ecklonia Cava Extract	Fresh, semidried *Ecklonia cava* seaweed is dried and crushed followed by alcohol (i.e., food-grade ethanol) extraction, purification, filtration, and concentration steps.	[9]
Ecklonia Cava Extract	Small pieces of *Ecklonia cava* fronds (~ 5 cm; 30 kg) are placed in 750 L of distilled water in the presence of enzymes (300 g pectinase and 300 g cellulase). Suspension is stirred for 24 h at 50°C, centrifuged at 3000 g for 20 min at 4°C, and vacuum filtered. Three volumes of 60% ethanol are then added for 18 h of extraction. Solution is filtered and concentrated using a rotary evaporator. Concentrated solution is made into powder using a spray dryer.	[21]
Ecklonia Cava Extract (high in polyphenols)	Dried *Ecklonia cava* powder is extracted with ethanol, concentrated, and freeze-dried.	[22]
Fucus Vesiculosus Extract (28.8% polyphenols)	Ethanol (30% - 35% aq.) extraction of *Fucus vesiculosus* (10% w/w) is performed at room temperature under mechanical stirring for 4 h. After filtration on a filter press, liquid phase undergoes an initial purification step to remove alginates by precipitation in presence of excess calcium chloride. Liquid phase undergoes a second purification step involving diafiltration to remove iodine and low molecular weight compounds. Extract is freeze-dried to obtain a powder extract.	[23]
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Ethanol (50% - 70% aq.) extraction of *Fucus vesiculosus* (10% w/w) is performed to solubilize a greater amount of carotenoids at room temperature under mechanical stirring for 2 h. After filtration on a filter press, liquid phase undergoes an initial purification step to remove alginates by precipitating them in presence of excess calcium chloride. After solid-liquid separation, a second extraction is performed under same conditions. Two liquid phases are then blended, submitted to diafiltration to remove iodine and low molecular weight compounds, and freeze-dried to obtain a powder extract.	[23]
Fucus Vesiculosus Extract	Dried plant material is extracted with water for 24 h, with stirring at room temperature. Residue is then removed by filtration to give a slightly brown colored extract.	[24]
Laminaria Digitata Extract (high in oligosaccharides)	An aqueous extraction is conducted followed by enzymatic depolymerization that breaks the polysaccharide into oligosaccharides (e.g., smaller polymers with 3 to 10 sugar components). Final process involves chelating oligosaccharide with zinc sulfate (0.1% zinc-pyrrolidone).	[25]
Laminaria Japonica Extract (low-molecular weight fucoidan)	Enzyme hydrolysis	[26]
Laminaria Japonica Extract	Plant is rinsed with tap water to remove salt and dried in an air dryer at 60°C for 40 h. Dried material is ground with a hammer mill, and powder stored at −20°C until used. Dried powder (2.5 kg) is extracted 3 times with 96% (v/v) ethanol for 3 h at 70°C. Combined extracts are filtered and concentrated under reduced pressure to obtain ethanol extracts	[27]
Laminaria Japonica Extract	Freshly collected plant material is air dried with a fan for 24 h then ground into a fine powder. 5 g of powder is added to 100 mL of 1:1 water:propylene glycol at room temperature for 1 day. This procedure is repeated 2 times, and the combined extracts were stored at −20°C until use.	[28]
Laminaria Japonica Powder	Dried plant is pulverized to desired size.	[29]
Sargassum Fusiforme Extract and Undaria Pinnatifida Extract (high in fucosterol and phytol)	Microwave-assisted extraction coupled with high-speed countercurrent chromatography.	[30]
Sargassum Fusiforme Extract and Undaria Pinnatifida Extract (high in lipids and antioxidant compounds)	Supercritical fluid extraction and subcritical water extraction.	[30]
Unidaria Pinnatifida Extract (high in fucoidan)	Plant material is hydrolyzed in 0.05 or 0.5 M hydrochloric acid at 80°C for 30 min then neutralized with 1 M sodium hydroxide. Resulting material is desalted by gel filtration and hydrolysate lyophilized.	[31]

aq. = aqueous; HPLC = high-performance liquid chromatography

Table 7. Constituents in brown algae.

Constituent(s)	Description
Alkaloids	Tyramine (TYR, 4-hydroxyphenylethylamine) has been detected in *Laminaria saccharina*.[97] The alkaloids found in marine algae may be divided into three groups: phenylethylamine alkaloids, indole and halogenated indole alkaloids, and other alkaloids.
Amino acids	Brown algae contain all of the essential amino acids and are greater in threonine, valine, leucine, lysine, glycine, and alanine than are the green and blue algaes.[30] *Fucus spiralis* was reported to contain 63.5% essential amino acids per total protein, containing leucine (5.5 mg/g protein), isoleucine (15.3 mg/g protein), lysine (12.5 mg/g protein), glutamic acid (12.1 mg/g protein), arginine (11.7 mg/g protein), serine (11.5 mg/g protein), valine (11.1 mg/g protein), and threonine (10.9 mg/g protein).[98]
Betaines	Glycinebetaine, γ-aminobutyric acid betaine, and/or trigonelline have been found in *Alaria esculenta*, *Ecklonia maxima*, *Ecklonia radiata*, *Eisenia arborea*, *Laminaria digitate*, *Macrocystis pyrifera*, *Nereocystis luetkeana*, *Saccharina angustata*, *Saccharina japonica*, and *Undaria pinnatifida*.[99]
Iodine	The concentration of iodine in *Alaria esculenta* was reported to have a range of approximately 200 mg/kg (dry wt) to approximately 700 mg/kg (dry wt) depending on year, season, location, and whether it was collected in the wild, a monoculture, or an integrated culture.[100] *Fucus vesiculosus* contains between 0.03% and 0.2% iodine in dried material.[101] The iodine content is highest in the spring in freshly cut young blades. In *Laminaria digitata*, iodine content is highest in late autumn and winter (0.75% to 1.20% dry wt) and lowest in summer (0.25% to 0.60% dry wt).[102] Iodine content for *Fucus spiralis* and *Laminaria ochroleuca* have been reported to be 232.7 and 883.5 mg/kg dry wt.[98]
Laminarins	Laminarins are basically a class of low molecular weight storage β-glucans. These are composed of (1,3)-β-D-glucan and can be up to 35% of the dry weight of brown algae.[103]
Lipids	Fucosterol and fucosterol derivatives are present in brown algae.[30] Fucoxanthine, tocopherols, and sterols are also found in brown algae.
Omega-3 fatty acids	Omega-3 fatty acids include stearidonic acid and hexadecatetraenoic acid.[104] These make up to 40% of the total fatty acid content in *Undaria pinnatifida*.
Phenolic compounds, polyphenols, and phlorotannins	Phlorotannins are found in brown algae.[30] Flavonoids are integral structural components of cell walls (e.g., eckol, phlorofucofuroeckol A, dieckol, catechin, and epigallocatechin).
Pheromones	The pheromones include lamoxirene 4 (e.g., *Agarum cribrosum*, *Ecklonia radiata*, *Eisenia arborea*, *Laminaria digitata*, *Laminaria hyperborea*, *Laminaria japonica*, *Laminaria saccharina*, *Saccharina angustata*, *Undaria pinnatifida*, *Macrocystis pyrifera*, and *Nereocystis luetkeana*), fucoserratene 6 (e.g., *Fucus serratus*, *Fucus spiralis*, and *Fucus vesiculosus*), hormonsirene 8 (e.g., *Durvillaea antarctica*), and finavarrene 12 (*Ascophyllum nodosum*). The major constituents of the essential oil of *Dictyopteris polypodioides* are C_{11} hydrocarbons sulfur products such as 3-hexyl-4,5-dithiacycloheptanone.[20]
Phytohormones	Auxins (plant hormones that cause the elongation of cells in shoots and are involved in regulating plant growth), such as indoleacetic acid are found in the genera *Macrocystis*, *Laminaria*, *Fucus*, *Ascophyllum*).[30,105] Cytokinins (genera *Fucus*, *Ascophyllum*, *Sargassum*, *Macrocystis*), gibberellins (genus *Fucus*), abscisic acid (genera *Ascophyllum*, *Laminaria*), and polyamines (genus *Dyctiota*) are also found.
Pigments	Carotenoids including fucoxanthin, β-carotene, zeaxanthin, violaxanthin, and antheraxanthin are found in brown algae.[30] These vary with season.
Protein	The protein content of algae varies according to species and season.[14,30] In general, the protein fraction of brown algae is low (1% to 24% dry wt.) compared with that of green or red algae (4% to 50% dry wt). Except for the species *Undaria pinnatifida*, which has a protein content between 11% and 24% (dry wt.), most commercial brown algae have a protein content lower than 15% (dry wt; e.g., *Ascophyllum nodosum*, 3% to 15%; *Fucus vesiculosus*, *Himanthalia elongate*, and *Laminaria digitata*, 8% to 15%). The protein content of *Fucus* sp. tend to range from 3% to 11% (e.g., *Fucus spiralis*, 9.71% dry weight).[98]
Sterols	Sterols found in brown algae include desmosterol, ergosterol, fucosterol, cholesterol, campesterol, stigmasterol, and β-sterol.[38,39]
Terpenoids	Terpenes, phenolic compounds, and meroterpenes make up the three major classes of secondary metabolites in brown seaweed.[30]

Table 8. **Constituents in *Ascophyllum nodosum*, *Fucus vesiculosus*, and *Laminaria digitate***

	Ascophyllum nodosum (ppm) [106]	*Fucus vesiculosus* (ppm) [107]	*Fucus vesiculosus* (ppm) [106]	*Laminaria digitate (ppm)* [25]
Algin	NR	41300 – 500000	NR	
Alginic acid	NR	NR	NR	200000 – 450000
Aluminum	NR	75.0 - 631.0	NR	
Arsenic	NR	68.0	NR	
Ascorbic-acid	NR	30.0 - 258.0	NR	
Bromine	NR	150.0	NR	
Calcium	9847	3587 – 30400	11600	
Carbohydrates	NR	77290 – 655000	NR	10000 – 20000
β-carotene	NR	5.0 – 40.0	NR	
Chromium	NR	0.1 – 0.7	NR	
Cobalt	NR	0.2 – 1.6	NR	
Fat	NR	3540 – 30000	NR	10000 – 20000
Fiber	NR	98000	NR	
Fiber(crude)	NR	98000	NR	
Fiber(dietary)	NR	482000	NR	
Fucinicacid	NR	1000	NR	
Fucoidin	NR	600000	NR	20000 – 40000
Fucose	NR	240000	NR	
Iodine	NR	64.0 – 540.0	NR	3000 – 1100
Iron	133.4	2.0 – 16.0	189.9	
Kilocalories	NR	2490	NR	
Lead	NR	91.0	NR	
γ-Linolenic acid	NR	NR	NR	
Magnesium	8678	1023 – 8670	7320	5000 – 8000
Mannitol	NR	NR	NR	40000 – 160000
Manganese	19.6	0.9 – 7.6	82.8	
Mercury	NR	40.0	NR	
Niacin	NR	6.0 – 47.0	NR	
Phosphorus	NR	294.0 -2490	1935.7	
Potassium	37810	2490 – 21,100	37450	13000 – 38000
Selenium	NR	0.2 – 1.7	NR	
Silicon	NR	0.9 – 7.6	NR	
Sodium	45757	6620 – 56,100	21875	9000 – 22000
Sugars	NR	2360 – 20000	NR	
Tin	NR	3.0 – 24.0	NR	
Water	NR	882000	NR	730000 – 900000
Zinc	NR	0.1 – 0.6	NR	

NR = not reported

Table 9. **Sterols in several brown algae**

Species	Desmosterol (mg/kg)	Ergosterol (mg/kg)	Fucosterol (mg/kg)	Cholesterol (mg/kg)	Campesterol + Stigmasterol (mg/kg)	β-Sterol (mg/kg)	Brassicasterol (mg/kg)	Ssaringosterol (mg/kg)	24-ketocholesterol (mg/kg)	Total[a] (mg/kg)	Reference
Cystoseira tamariscifolia	44.1 ± 3.4	-	5260.2 ± 14.9	500.4 ± 2.6	680.9 ± 21.4	17.0 ± 0.3	NR	NR	NR	6502.6	[39]
Fucus spiralis	37.6 ± 3.8	-	3815.1 ± 329.5	325.1 ± 13.5	183.4 ± 0.3	-	NR	NR	NR	4361.0	[39]
Sargassum vulgare	47.2 ± 0.2	5.6 ± 0.4	4451.5 ± 16.7	406.3 ± 13.2	303.3 ± 18.9	15.2 ± 2.8	NR	NR	NR	5229.1	[39]

NR = not reported; - = not found

[a] Total may not be exact due to rounding.

Table 10. **Constituents of ethanol extracts of *Fucus spiralis* and *Sargassum vulgare*.**[41]

	Range (if provide; ppm)	
Constituent	***Fucus spiralis* extract**	***Sargassum vulgare* extract**
Arachidic Acid	ND	ND
Arachidonic Acid	465.6 ± 29.0	ND
Cholesterol	ND	127.4 ± 11.6
Eicosapentaenoic Acid	217.0 ± 11.4	ND
Fucosterol	317.6 ± 9.4	257.6 ± 43.6
γ-Linolenic Acid	ND	2413.6 ± 57.6
Mannitol (Total)	1273.8 ± 34.8	394.6 ± 15.2
Myristic Acid	69.8 ± 2.7	ND
Palmitic Acid	606.0 ± 20.6	340.4 ± 95.0
Phloroglucinol	< LOD	ND
Proline	396.8 ± 96.8	117.4 ± 11.0
β-Sitosterol	ND	ND
Stearic Acid	208.4 ± 21.4	204.0 ± 26.0
Vaccenic Acid	21,690.6 ± 1667.6	2848.6 ± 71.2

LOD = limit of detection; ND = not detected

Table 11. **Composition of a 50/50 water/propylene glycol extract of *Laminaria japonica*[28]**

Constituent	**Amount**
Constituent Groups (mg/g)	
Carbohydrate	6
Sugars	5
Proteins	2
Crude fat	2
Saturated fatty acid	1
Unsaturated fatty acid	None detected
Amino Acids (mg/L)	
Alanine	42.3
Ammonium chloride	16.2
Arginine	20.3
Aspartic acid	424.7
Glutamic acid	689.4
Glycine	1.7
Hydroxyproline	381.4
Phosphoserine	3.7
Serine	8.6
Threonine	4.2
Minerals (mg/g)	
Sodium	404
Calcium	300
Potassium	1022
Magnesium	35
Iron	0.5
Zinc	0.2

Table 12. **Composition of enzyme hydrolysis extracts of *Laminaria japonica*[26]**

Constituent	Concentration (% w/w)
	***Laminaria japonica* extract**[26]
Ash	4.1 ± 0.1
Fat	0.6 ± 0.1
Fucose	85.9
Moisture	3.9 ± 0.8
Monosaccharides (neutral)	NR
Protein	4.3 ± 0.3%
Sulfate	28.4 ± 2.1

NR = not reported

Table 13. **Specifications of an alcohol extract of *Ecklonia cava* for use as a food supplement**[9]

Parameter	Specification
Phlorotannin	90 ± 5.0%
Dieckol	6.6% – 9.9%
Moisture content	< 5%
Ash	< 5%
Insoluble substances	Negative
Substances not originating from *E. cava*	Negative
Viable cell count	< 3000 CFU/g
Staphylococcus aureus	Negative
Molds and yeasts	< 300 CFU/g
Salmonella spp.	Negative
Coliforms	Negative
Lead	< 3 mg/kg
Mercury	< 0.1 mg/kg
Cadmium	< 3 mg/kg
Arsenic	< 25 mg/kg
Iodine	150.0 – 650.0 mg/kg
Sieving size	> 60 (0.250 mm)

Table 14. **Constituents of desalinated Undaria pinnatifida powder.**[42]

Constituent	Amount (mg/g)
Ash	147
Calcium	13.6
Copper	0.00130
Dietary fiber	532
Iron	0.107
Lipid	14
Magnesium	13.4
Protein	209
Sodium	25.4
Zinc	0.02

Table 15. **Amount of arsenic found in several brown algae species.**[33]

Species	Arsenic Concentration (mg/kg wet wt.)	Arsenic Concentration (mg/kg dry wt.)
Ecklonia radiate	10[33]	-
Hizikia fusiforme	10[33]	-
Laminaria japonica	4[33]	-
Laminaria ochroleuca	-	56.8 ± 2.4[43]
Laminaria saccharina	-	52.4 ± 2.1[43]
Saccharina (spp)	-	< 0.3[108]
Sargassum fusiforme	-	67 - 96[108]
Sargassum thunbergii	4[33]	-
Unidaria pinnatifida	2.8 – 4.5[33]	< 0.3[108] 115 ± 9[43]

- = no data

Table 16. **Arsenic -containing moieties found in various brown algae**[43]

	Amount (mg/kg)			
Arsenic-Containing Moiety	***Laminaria ochroleuca***	***Laminaria saccharina***	***Sargassum fulvellum***	***Undaria pinnatifida***
Arsenic III	ND	ND	ND	ND
Arsenic V	ND	ND	69.9 ± 1.0	0.29 ± 0.03
Methylarsonate	ND	0.21 ± 0.03	ND	ND
Dimethylarsinate	0.26 ± 0.08	0.67 ± 0.02	2.1 ± 0.1	0.13 ± 0.03
Trimethylarsine oxide	ND	ND	ND	ND
Arsenobetaine	0.20 ± 0.02	0.09 ± 0.02	ND	ND
Phospate-sug po4	6.2 ± 0.1	6.9 ± 0.1	2.2 ± 0.1	0.30 ± 0.02
Sulfonate-sug so3	39.4 ± 1.6	30.7 ± 1.2	1.80 ± 0.10	ND
Sulfate-sug so4	ND	ND	9.0 ± 0.7	ND
Glycerol-sug gly	2.71 ± 0.04	2.9 ± 0.1	1.2 ± 0.2	0.87 ± 0.03
Arsenocholine	ND	ND	ND	ND
Inorganic arsenic	ND	ND	69.9	0.29

ND = not detected

Table 17. **Arsenic species found in *Laminaria japonica* and an extract of *Laminaria japonica***[26]

	Amount (mg/kg)	
Arsenic Species	*Laminaria japonica*	*Laminaria japonica* extract[a]
Arsenic III	ND	ND
Arsenic V	ND	ND
Monomethylarsonic Acid	9.27 ± 0.96	1.35 ± 0.63
Dimethylarsinic Acid	9.23 ± 0.83	ND
Arsenobetaine	34.31 ±1.21	4.77 ± 0.88
Arsenocholine	6.19 ± 2.17	ND
Arsenic (sum)	59.00 ± 1.65	6.12 ± 2.005

ND = not detected

[a] Extracted by enzyme hydrolysis, high in low-molecular-weight fucoidan

Table 18. **Heavy metals in brown algae species**[44]

	Concentration of heavy metals (mg/kg dry weight)							Reference
Species	**Cadmium**	**Lead**	**Mercury**	**Copper**	**Zinc**	**Arsenic**	**Inorganic Arsenic**	
Alaria esculenta	0.22 – 7.9	0.2 – 1.9	< 0.005 - <0.071	0.39 - 4	7 - 45	<0.074 - 100	-	[109]
Fucus vesiculosus	1.7	11	-	12.7	89	13.5	-	[88]
Himanthalia elongate	0.310 – 0.326	0.203 – 0.259	0.008 – 0.016	1.14 – 1.25	48.5 – 48.7	32.9 – 36.7	0.166 – 0.245	[44]
Hizikia fusiforme	0.988 – 2.50	< 0.008[a] – 0.531	0.015 – 0.050	1.78 – 7.70	4.72 – 19.5	103 – 147	32.1 – 69.5	[44]
Laminaria spp.	0.085 – 1.83	< 0.008[a] – 0.460	0.001 – 0.005	0.91 – 2.50	10.3 – 23.2	51.7 – 68.3	0.052 – 0.443	[44]
Undaria pinnatifida	0.267 – 4.82	< 0.008[a] – 1.28	0.010 – 0.057	1.07 – 1.70	8.25 – 26.6	42.1 – 76.9	0.045 – 0.346	[44]

[a] Limit of detection.

spp. = multiple species

Table 19. **Frequency of use according to duration and exposure of brown algae-derived ingredients.**[48-50]

Use type	# Uses	Max. Conc. (%)	Uses	Max. Conc.(%)	Uses	Max. Conc.(%)	Uses	Max.Conc. (%)
	Agarum Cribrosum Extract		**Alaria Esculenta Extract**		**Ascophyllum Nodosum Extract**		**Ascophyllum Nodosum Powder**	
Total/range	**NR**	**0.012**	**37**	**0.0005-1**	**120**	**0.0000004-0.2**	**4**	**NR**
Duration of use[a]								
Leave-on	*NR*	*0.012*	*37*	*0.0005-1*	*91*	*0.0000004-0.2*	*3*	*NR*
Rinse-off	*NR*	*NR*	*NR*	*0.0015*	*29*	*0.00004-0.0032*	*NR*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*1*	*NR*
Exposure type								
Eye area	NR	NR	11	NR	16	0.025-0.2	NR	NR
Incidental Ingestion	NR	NR	3	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	3[a]; 6[b]	0.0005[a]	23[a]; 44[b]	0.002[a]	2[a]	NR
Incidental Inhalation-Powder	NR	NR	6[b]	0.0015-0.05[c]	1; 44[b]	0.0000004-0.03[c]	NR	NR
Dermal Contact	NR	0.012	33	0.0005-1	104	0.0000004-0.2	4	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Non-Coloring	NR	NR	1	NR	13	0.00005-0.002	NR	NR
Hair- Coloring	NR	NR	NR	NR			NR	NR
Nail	NR	NR	NR	NR	3	0.000065-0.02	NR	NR
Mucous Membrane	NR	NR	3	NR	6	0.00004	1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Cladosiphon Okamuranus Extract		**Dictyopteris Polypodioides Extract**[d]		**Durvillaea Antarctica Extract**		**Ecklonia Radiata Extract**	
Total/range	**9**	**0.005-0.05**	**1**	**0.01**	**NR**	**0.0001**	**NR**	**0.005-0.0051**
Duration of use								
Leave-on	*8*	*0.025-0.05*	*1*	*0.01*	*NR*	*0.0001*	*NR*	*0.0051*
Rinse-off	*1*	*0.005*	*NR*	*NR*	*NR*	*NR*	*NR*	*0.005*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure type								
Eye area	1	0.025	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	0.01	NR	NR	NR	NR
Incidental Inhalation-Spray	3[a]; 3[b]	NR	1[b]	NR	NR	NR	NR	0.0051
Incidental Inhalation-Powder	3[b]	0.025[b]	1[b]	NR	NR	NR	NR	NR
Dermal Contact	9	0.005-0.05	1	NR	NR	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair-Non-Coloring	NR	NR	NR	NR	NR	NR	NR	0.0051
Hair- Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	0.001	NR	NR
Mucous Membrane	NR	NR	NR	0.01	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Fucus Serratus Extract		**Fucus Vesiculosus**		**Fucus Vesiculosus Extract**		**Fucus Vesiculosus Powder**	
Total/range	**8**	**0.00001-0.05**	**NR**	**0.0003-0.0051**	**287**	**0.00002-6**	**3**	**NR**
Duration of use								
Leave-on	*8*	*0.05*	*NR*	*0.00098-0.0051*	*201*	*0.000032-6*	*1*	*NR*
Rinse-off	*NR*	*0.00001-0.05*	*NR*	*0.0003*	*75*	*0.00002-5*	*2*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*11*	*0.0001-5*	*NR*	*NR*
Exposure type								
Eye area	8	0.05	NR	NR	6	0.01-5	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	0.0005	NR	NR
Incidental Inhalation-Spray	3[a]; 4[b]	NR	NR	0.00098	1; 90[a]; 82[b]	0.00018-0.12; 0.0001-0.1[a]	1[b]	NR
Incidental Inhalation-Powder	4[b]	0.05[c]	NR	NR	82[b]	0.000032-6[c]	1[b]	NR
Dermal Contact	8	NR	NR	0.00098-0.0051	262	0.00002-6	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	NR	0.000010	NR	0.0003	22	0.0001-5	NR	NR
Hair- Coloring	NR	NR	NR	NR	NR	0.0001-0.001	NR	NR
Nail	NR	NR	NR	NR	NR	0.02	NR	NR
Mucous Membrane	NR	NR	NR	NR	30	0.00002-5	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 19. Frequency of use according to duration and exposure of brown algae-derived ingredients.[48-50]

Use type	# Uses	Max. Conc. (%)	Uses	Max. Conc.(%)	Uses	Max. Conc.(%)	Uses	Max.Conc. (%)
	Himanthalia Elongata Extract		**Laminaria Cloustoni Extract**		**Laminaria Digitata Extract**		**Laminaria Digitata Powder**	
Total/range	**9**	**NR**	**14**	**NR**	**235**	**0.00004-5**	**21**	**40**
Duration of use								
Leave-on	*7*	*NR*	*10*	*NR*	*162*	*0.0001-5*	*2*	*40*
Rinse-off	*2*	*NR*	*4*	*NR*	*66*	*0.00004-5*	*16*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*7*	*0.1-5*	*3*	*NR*
Exposure type								
Eye area	1	NR	1	NR	15	0.0035-0.5	NR	NR
Incidental Ingestion	NR	NR	NR	NR	2	NR	NR	NR
Incidental Inhalation-Spray	1[a]; 4[b]	NR	4[a]; 4[c]	NR	1; 44[a]; 67[c]	0.0007; 0.0035-5[a]	1[b]	NR
Incidental Inhalation-Powder	4[b]	NR	4[c]	NR	3; 67[c]	0.0001-0.1[c]	1[b]	40[b]
Dermal Contact	7	NR	14	NR	191	0.0001-5	15	40
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	2	NR	NR	NR	36	0.0007-5	6	NR
Hair- Coloring	NR	NR	NR	NR	1	0.00004-0.0007	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	20	0.06-5	4	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Laminaria Hyperborea Extract		**Laminaria Japonica Extract**		**Laminaria Ochroleuca Extract**		**Laminaria Saccharina Extract**	
Total/range	**2**	**0.03**	**77**	**0.005-5**	**26**	**0.000024-0.63**	**132**	**0.00001-0.54**
Duration of use								
Leave-on	*2*	*0.03*	*62*	*0.0005-5*	*22*	*0.00017-0.63*	*85*	*0.000092-0.54*
Rinse-off	*NR*	*NR*	*15*	*0.0005-5*	*4*	*0.000024-0.017*	*47*	*0.00001-0.51*
Diluted for (bath) use	*NR*	*NR*	*NR*	*0.011-5*	*NR*	*NR*	*NR*	*NR*
Exposure type								
Eye area	NR	NR	3	0.0005-0.007	2	0.0034-0.63	NR	0.000092-0.019
Incidental ingestion	NR	NR	1	NR	1	NR	NR	NR
Incidental Inhalation-Spray	2[a]	NR	7[a]; 28[b]	0.3-5[a]	3[a]; 5[b]	0.017; 0.017[a]	40[a]; 19[c]	0.001-0.005
Incidental Inhalation-Powder	NR	0.03[c]	3; 1[c]; 28[b]	0.0035; 0.0055-5[c]	3; 5[b]	0.0005-0.17[c]	19[c]	0.0008; 0.000092-0.1[c]
Dermal Contact	2	0.03	72	0.0005-5	25	0.000024-0.63	120	0.000092-0.54
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	0.15[e]
Hair- Non-Coloring	NR	NR	1	0.0005-0.3	NR	0.017	12	0.00001-0.045
Hair- Coloring	NR	NR		NR	NR	0.017	NR	
Nail	NR	NR	2	NR	NR	NR	NR	0.001
Mucous Membrane	NR	NR	3	0.011-5	3	NR	4	0.51
Baby Products	NR	NR	1	NR	NR	NR	NR	NR

	Lessonia Nigrescens Extract		**Macrocystis Pyrifera (Kelp)**		**Macrocystis Pyrifera (Kelp) Extract**		**Macrocystis Pyrifera (Kelp) Protein**	
Total/range	**NR**	**0.032**	**2**	**NR**	**188**	**0.00005-36.4**	**3**	**NR**
Duration of use								
Leave-on	*NR*	*NR*	*1*	*NR*	*106*	*0.0002-36.4*	*1*	*NR*
Rinse-off	*NR*	*0.032*	*1*	*NR*	*78*	*0.00005-5*	*2*	*NR*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*4*	*0.0051-1*	*NR*	*NR*
Exposure type								
Eye area	NR	NR	NR	NR	5	0.007-36.4	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	0.079	NR	NR
Incidental Inhalation-Spray	NR	NR	1[a]	NR	9; 38[a]; 26[b]	0.042-0.79; 0.0036-5[a]; 0.17[b]	NR	NR
Incidental Inhalation-Powder	NR	NR	NR	NR	2; 26[b]	0.0035; 0.001-33.3[c]; 0.17[b]	NR	NR
Dermal Contact	NR	0.032	2	NR	123	0.00005-36.4	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	NR	NR	NR	NR	56	0.001-5	NR	NR
Hair- Coloring	NR	NR	NR	NR	4		NR	NR
Nail	NR	NR	NR	NR	5	0.0002-0.0011	NR	NR
Mucous Membrane	NR	NR	1	NR	34	0.0051-5	1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 19. **Frequency of use according to duration and exposure of brown algae-derived ingredients.**[48-50]

Use type	# Uses	Max. Conc. (%)	Uses	Max. Conc.(%)	Uses	Max. Conc.(%)	Uses	Max.Conc. (%)
	Pelvetia Canaliculata Extract		**Sargassum Filipendula Extract**		**Sargassum Fusiforme Extract**		**Sargassum Muticum Extract**	
Total/range	**47**	**0.00002-0.018**	**46**	**0.0001-1.2**	**7**	**NR**	**1**	**0.01-4**
Duration of use								
Leave-on	*34*	*0.00002-0.018*	*14*	*0.0001-1.2*	*4*	*NR*	*NR*	*2-4*
Rinse-off	*13*	*0.00004-0.0018*	*32*	*0.002-0.29*	*3*	*NR*	*1*	*0.01*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure type[a]								
Eye area	6	0.00002-0.0007	2	NR	NR	NR	NR	2.5-4
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1; 18[a]; 8[b]	0.00004-0.0007; 0.002-0.0035[a]	3; 5[a]; 1[b]	0.0001[a]	2[a]; 2[b]	NR	NR	NR
Incidental Inhalation-Powder	8[b]	0.002-0.018[c]	1[b]	0.8[c]	2[b]	NR	NR	NR
Dermal Contact	19	0.00002-0.018	16	0.002-1.2	7	NR	1	0.01-4
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	24	0.00004-0.0025	7	0.0001-0.29	NR	NR	NR	NR
Hair- Coloring	1	0.0000-0.0007	23	0.011-0.29	NR	NR	NR	NR
Nail			NR	NR	NR	NR	NR	NR
Mucous Membrane	1	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Sargassum Vulgare Extract		**Sphacelaria Scoparia Extract**		**Undaria Pinnatifida Extract**		**Undaria Pinnatifida Powder**	
Total/range	**NR**	**0.0075-0.016**	**8**	**0.016**	**74**	**0.00001-5**	**NR**	**0.1**
Duration of use								
Leave-on	*NR*	*0.009-0.016*	*6*	*0.016*	*64*	*0.00001-5*	*NR*	*NR*
Rinse-off	*NR*	*0.0075*	*2*	*NR*	*10*	*0.0001-5*	*NR*	*0.1*
Diluted for (bath) use	*NR*	*NR*	*NR*	*NR*	*NR*	*0.0001*	*NR*	*NR*
Exposure type								
Eye area	NR	0.011	NR	NR	4	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	0.009[a]	1[a]; 4[c]	NR	12[a]; 38[b]	0.002[a]	NR	NR
Incidental Inhalation-Powder	NR	0.011[c]	4[c]	NR	3; 38[b]	0.00001-5; 0.00001-5[c]	NR	NR
Dermal Contact	NR	0.011-0.016	8	0.016	68	0.00001-5	NR	0.1
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair- Non-Coloring	NR	0.0075-0.009	NR	NR	6	0.002-5	NR	NR
Hair- Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	2	NR	4	0.0001	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Kelp[f]		**Kelp Extract**[f]		**Laminaria Extract**[f]	
Total/range	**24**	**NS**	**15**	**NS**	**4**	**NS**
Duration of use						
Leave-on	*9*	*NS*	*10*	*NS*	*2*	*NS*
Rinse-off	*10*	*NS*	*4*	*NS*	*2*	*NS*
Diluted for (bath) use	*5*	*NS*	*1*	*NS*	*NR*	*NS*
Exposure type						
Eye area	NR	NS	1	NS	NR	NS
Incidental Ingestion	1	NS	NR	NS	NR	NS
Incidental Inhalation-Spray	3[a]; 3[b]	NS	5[a]; 1[b]	NS	1[b]	NS
Incidental Inhalation-Powder	3[b]	NS	1[b]	NS	1[b]	NS
Dermal Contact	19	NS	8	NS	2	NS
Deodorant (underarm)	NR	NS	NR	NS	NR	NS
Hair- Non-Coloring	4	NS	7	NS	2	NS
Hair- Coloring	NR	NS	NR	NS	NR	NS
Nail	NR	NS	NR	NS	NR	NS
Mucous Membrane	11	NS	2	NS	NR	NS
Baby Products	NR	NS	NR	NS	NR	NS

NR = Not Reported; NS = Not Surveyed; Totals = Rinse-off + Leave-on + Diluted for Bath Product Uses.
Note: Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure type uses may not equal the sum total uses.
[a] It is possible these products may be sprays, but it is not specified whether the reported uses are sprays.
[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.
[c] It is possible these products may be powders, but it is not specified whether the reported uses are powders.
[d] Frequency of use and concentration of use were reported under the INCI name Dictyopteris Membranacea Extract (Retired).
[e] Not spray.
[f] Reported in the VCRP under a non-INCI name and presented here for information purposes.

Table 20. Brown algae-derived ingredients with no reported uses in the VCRP or the Council survey.[48-50]

Ascophyllum Nodosum	Asterionellopsis Glacialis Extract	Cladosiphon Novae-Caledoniae Extract
Cystoseira Amentacea/Caespitosa / Branchycarpa Extract	Cystoseira Baccata Extract	Cystoseira Balearica Extract
Cystoseira Caespitosa Extract	Cystoseira Compressa Extract	Cystoseira Compressa Powder
Cystoseira Tamariscifolia Extract	Dictyota Coriacea Extract	Ecklonia Cava Extract
Ecklonia Cava Water	Ecklonia Kurome Extract	Ecklonia Kurome Powder
Ecklonia/Laminaria Extract	Ecklonia Maxima Extract	Ecklonia Maxima Powder
Eisenia Arborea Extract	Fucus Spiralis Extract	Halidrys Siliquosa Extract
Halopteris Scoparia Extract	Himanthalia Elongata Extract	Himanthalia Elongata Powder
Hizikia Fusiforme Extract	Hizikia Fusiformis Water	Hizikia Fusiformis Callus Culture Extract
Hydrolyzed Ecklonia Cava Extract	Hydrolyzed Fucus Vesiculosus Extract	Hydrolyzed Fucus Vesiculosus Protein
Laminaria Diabolica Extract	Laminaria Japonica Powder	Laminaria Longissima Extract
Lessonia Nigrescens Powder	Macrocystis Pyrifera (Kelp) Blade/ Pneumatocyst/Stipe Juice Extract	Macrocystis Pyrifera (Kelp) Juice
Nereocystis Luetkeana Extract	Pelvetia Siliquosa Extract	Phyllacantha Fibrosa Extract
Rissoella Verruculosa Extract	Saccharina Angustata Extract [Laminaria Angustata Extract (Retired)]	Saccharina Japonica Extract [Laminaria Ochotensis Extract (Retired)]
Saccharina Longicruris Extract	Sargassum Fulvellum Extract	Sargassum Glaucescens Extract
Sargassum Horneri Extract	Sargassum Pallidum Extract	Sargassum Siliquastrum Extract
Sargassum Thunbergii Extract	Sahel Scenedesmus Extract	Undaria Peterseniana Extract
Undaria Pinnatifida Cell Culture Extract	Undaria Pinnatifida Leaf/Stem Extract	Undaria Pinnatifida Root Powder

Table 21. Acute oral toxicity studies

Ingredient	Animals	No./Group	Vehicle	Concentration/Dose/Protocol	LD_{50}/Results	Reference
				ORAL		
Cystoseira Compressa Extract (methanol, hexane, and chloroform extracts)	Albino mice	2	Not specified	Up to 2000 mg/kg by gavage. Observed for 24 h.	There were no mortalities or clinical signs for any of the extracts.	40
Ecklonia Cava Extract (alcohol extract)	Sprague-Dawley (Crl:DC(DS)) rats	10/sex	Not specified	2000 mg/kg by gavage. Observed for 2 weeks.	There were no mortalities. Clinical signs were soft stools, diarrhea, mucus stools, compound-colored feces, and soiled perineal region from the day of administration until day 2.	9
Ecklonia Cava Extract (enzyme extract)	SD rats	5/sex	Distilled water	0 or 3000 mg/kg by oral gavage. Rats were observed for 14 days.	No abnormal changes in body weights, clinical signs, or mortalities were observed. Necropsy results showed no macroscopic lesions in any organs of treatment group.	21
Ecklonia Cava Extract (enzyme extract)	Beagle dogs	2/sex	Distilled water	3000 mg/kg by oral gavage in two equally divided doses approximately 6 h apart. Dogs were observed for 14 days.	No abnormal changes in body weights, clinical signs, or mortalities were observed. Necropsy results showed no macroscopic lesions in any organs of treatment group.	21
Fucus Vesiculosus Extract (28.8% polyphenols)	Swiss mice	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. An Irwin test (determines the general effects of a test substance on the central nervous system and physiological functions) was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Mice were observed for 7 days.	LD_{50}: Males = 1000 mg/kg; females = between 1000 and 2000 mg/kg	23
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Swiss mice	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. Irwin test was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Mice were observed for 7 days.	LD_{50}: Males = 500 mg/kg; females = < 750 mg/kg	23
Fucus Vesiculosus Extract (28.8% polyphenols)	Sprague-Dawley rats	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. Irwin test was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Rats were observed for 7 days.	LD_{50}: Males and females = between 1000 and 2000 mg/kg	23
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Sprague-Dawley rats	7/sex	1% carboxymethyl-cellulose	1000 - 2000 mg/kg OECD GL 425 Administered by gavage. Irwin test was performed at 1 and 5 h after administration of the extracts to detect motor, respiratory, temperature, circulatory, behavior, or other alterations. Rats were observed for 7 days.	LD_{50}: Males and females = > 2000 mg/kg	23
Sargassum Fulvellum Extract (dichloromethane, ethanol, and water extracts)	BALB/c mice	5	Tween-80 (5%)	5000 mg in 10 ml vehicle by gavage. Observed for 2 weeks.	There were no mortalities. Most of the mice reacted immediately by perpetual gagging, jumping, sleeping, scaling, and writhing for 5–10 min.	63

OECD GL = Organisation for Economic Co-operation and Development Guidelines

Table 22. Oral repeated dose studies

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference
			Short-Term				
Ascophyllum nodosum	Dried	Topigs Hybrid X Piétrain weanling pigs (20)	23 days	Feed	0, 2.5, 5.0, or 10.0 g/kg feed (0.25%, 0.5%, or 1.0%)	There were no adverse effects from treated feed. There were no effects on weight gain, feed consumption. Digestion characteristics were similar to controls (pH, fresh matter weight, and dry matter content), except for pH of part of the intestine was increased in the high-dose group (6.28 vs.5.96).	[110]
Ascophyllum nodosum	Freeze-dried and powdered	Male Sprague-Dawley rats (6)	4 weeks	Feed	0, 5%, 10%, or 15% in feed	Food intake, weight gain, and serum enzyme (alanine transaminase and aspartate transaminase) levels indicated that seaweed diets were well tolerated.	[111]
Ecklonia Cava Extract	Alcohol extract	Male ICR mice (10)	4 weeks	None	0, 1.25, 2.5 or 5 mg/day Mice were fed high fat diet (20% fat) or normal diet (5% to 10% fat). After 1 week, mice in high fat diets were administered Ecklonia Cava Extract by gavage while continuing on the high fat diet.	There were no mortalities. There was a dose-dependent lower body weight of ~ 12% - ~ 16% in the mice administered the extract compared to control group. Triglycerides, total cholesterol and LDL cholesterol were decreased in all treated groups. Liver enzymes (GPT and GOT), BUN, and creatinine values in serum were similar to controls. No data on feed consumption provided.	[64]
Ecklonia Cava Extract	Enzyme extract	SD rats (5/sex)	14 days	Water	0, 1000, 2000, or 5000 mg/kg by gavage	- There were no mortalities. No dose-related clinical abnormalities or body weight changes. - Macroscopic examination did not reveal any treatment-related abnormal lesions in males or females at necropsy; although redness in thymus, red spot in lung, and congestion and red spot in cervical lymph node were sporadically observed without a dose-dependent relationship. - Females in the 2000 and 5000 mg/kg groups had decreases in absolute and relative left ovary weights relative to control group and decreases in absolute brain weights were observed in females in 5000 mg/kg group.	[21]
Ecklonia Cava Extract	Alcohol extract	Sprague-Dawley (Crl:CD(SD)) rats (5/sex)	4 weeks	None	0, 500, 1000, or 2000 mg/kg/day by gavage.	- Compound-colored stools were observed in all rats in all dosing groups starting from day 1 of dosing. Salivation after dosing was observed sporadically in 1 female in the 1000 mg/kg/day group and in 2 males and 2 females in the 2000 mg/kg/day group on days 5 to 17 of dosing. - In clinical chemical investigations in 2000 mg/kg/day group, increases in ALT, and decreases in total protein, triglycerides and glucose were observed in males. Absolute and relative liver weights and absolute kidney weights were increased in males in 2000 mg/kg/day group. In females, relative heart weights were decreased in 1000 and 2000 mg/kg/day groups. There were no differences between study groups concerning body weight. Histopathologically, atrophy of periportal hepatocytes in livers was detected in male rats in 2000 mg/kg/day group.	[9]
Ecklonia Cava Extract	Alcohol extract	Beagle dogs (2/sex)	8 days 2-week observation period	Capsule	Day 1, 100 mg/kg; Day 4, 300 mg/kg; and day 8, 1000 mg/kg	There were no mortalities. Compound-colored stools were observed in all dogs in 300 and 1000 mg/kg groups. Vomiting was observed in 1 male and 1 female dog when treated at 1000 mg/kg.	[9]

Table 22. Oral repeated dose studies

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference
Ecklonia cava powder (inference for Ecklonia Cava Extract and Ecklonia Cava Water)	Freshly collected fronds were dried and powdered	Landrace x Yorkshire x Duroc weanling pigs (50)	28 days	In feed (growing-finishing diet)	0%, 0.05%, 0.1%, or 0.15% in feed	No mortalities. Weight gain was similar to controls. No significant effect on serum level of IgG, IgA, and IgM.	65
Fucus Vesiculosus Extract (28.8% polyphenols)	Ethanol (30% - 35% aq)	Sprague-Dawley rats (7/sex)	4 weeks	1% CMC	0, 200, or 750 mg/kg/day by gavage	- There were no mortalities. -Males: body and most organ weights were similar to controls. Livers had an increase weight (21%) at necropsy. - Females: body and organ weights were similar to controls.	23
Fucus Vesiculosus Extract (18% polyphenols plus 0.0012% fucoxanthin)	Ethanol (50% - 70% aq.)	Sprague-Dawley rats (7/sex)	4 weeks	1% CMC	0, 200, or 750 mg/kg/day by gavage	- There were no mortalities. - Males: body and most organ weights were similar to controls. Livers had an increase weight (25%) at necropsy. - Females: body and organ weights were similar to controls.	23
Laminaria Japonica Extract	Ethanol extract	Sprague-Dawley rats (6)	6 weeks	Not clear (probably daily gavage)	0, 100, 200, or 400 mg/kg starting after 6 weeks of a 12-week high-fat diet	- There were no mortalities. - Treatment groups had decreased the body weight gain, fat-pad weights, and serum and hepatic lipid levels in high-fat-induced obese rats. Histological analysis showed that treated groups had decreased number of lipid droplets and size of adipocytes compared to untreated high-fat diet group.	27
				Subchronic Oral			
Ecklonia Cava Extract	Alcohol extract	Sprague–Dawley (Crl:CD(SD)) rats (10/sex;5 additional in control and high-dose groups)	13 weeks 4-week recovery period for 5 rats in control and high-dose group	Water	0, 375, 750, or 1500 mg/kg/day	- Compound-colored stools in all dose levels; not considered to be of toxicological significance. -At 750 and 1500 mg/kg/day, BUN was decreased in males, glucose was decreased in females, and neutrophil counts were increased in females, compared to controls. Sporadic salivation occurred in females. - At 1500 mg/kg/day, incidence of salivation in females increased and occurred in male rats. Salivation was mainly observed after gavage, but to some degree also before. It was considered by authors to be a temporary sign caused by the test substance, since it was no longer evident later in the day. Number of rats with salivation increased with study duration. -At 1500 mg/kg/day, males and females had a lower body weight (11.7% and 8.7%, respectively) at end of study compared to controls (not statistically significant). This effect was dose related, appearing to a minor degree also at lower dose levels. Body weight effects were more pronounced in recovery group in both sexes. Feed consumption was not decreased. Blood chemistry analyses showed increases of phosphorus and ALT concentrations and a decrease of triglycerides in males, and a decrease of glucose in females, compared to controls. Prothrombin time was increased in males compared to controls. These changes were not evident after recovery period. There were no compound related findings in histopathological investigations including liver.	9

Table 22. **Oral repeated dose studies**

Test Article	Extraction Solvent/Method or Composition	Animals (n)	Study Duration	Vehicle	Dose/ Concentration	Results	Reference
Ecklonia Cava Extract	Enzyme extract	SD rats (5/sex)	13 weeks	Water	0, 500, 1000, 2000, or 3000 mg/kg by gavage	- There were no mortalities. None of groups had any dose-related clinical abnormalities or body weight changes. - Urinalysis and hematological analysis showed no treatment-related adverse effects. - Serum biochemistry and organ weights showed sporadic changes. However, sporadic changes might not have any relationship with treatment because these changes were very minimal within physiologically acceptable ranges without consistency between male and female rats. - Gross visual and macroscopic changes were not observed in organs of treated rats. Histopathological examination of sampled organs revealed a few spontaneous lesions which might be unrelated to treatment because there was no difference in incidence between control and treatment groups.	[21]
				Chronic Oral			
Laminaria Japonica Powder	Dried and powdered	Male CDF1 mice (6)	Life time	Feed	0, 2%, 5%	Mean lifespans were similar in all groups: 907 ± 135, 746 ± 183, and 851 ± 225 days for 0, 2%, and 5%, respectively.	[29]
Undaria Pinnatifida Extract	Filtered aqueous extract of powdered stems and thick leaves (1.5 g in 1000 ml distilled water)	Female Sprague-Dawley (SD) rats (12)	32 weeks	As drinking water	0 or 100% for water	There were no mortalities. Body weight changes were similar between groups.	[66]
Undaria Pinnatifida Powder	Dried and ground	Female SD rats (5)	36 weeks	Feed	0, 1.0%, or 5.0%	There were no mortalities. Body weight changes, thyroid weights, and T4 levels were similar between groups.	[74]

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AMP = adenosine monophosphate; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CMC = carboxymethylcellulose; GOT = glutamic oxaloacetic transaminase; GPT = glutamic pyruvic transaminase; HDL = high-density lipoprotein; IgA = immunoglobulin A; IgG = immunoglobulin G; IgM = immunoglobulin M; LDL = low-density lipoprotein; MCHC = mean corpuscular hemoglobin concentration; T4 = thyroxin

Table 23. Genotoxicity studies

Ingredient/Test Article	Extraction Solvent/ Method	Concentration/ Vehicle	Procedure	Test System	Results	Reference
			In Vitro			
Ascophyllum Nodosum Extract	Not specified	50, 150, 500, 1500, or 5000 µg/plate; in water	Ames assay, with and without metabolic activation in accordance with OECD GL 471 (bacterial reverse mutation test). Negative control: histidine; positive control: 4-nitroquinoline-N-oxide, 3-methylmethane sulphonate, 2-aminoanthracene, and sodium azide. There was no solvent control.	*S. typhimurium* (strains TA97, TA98, TA100, TA102, and TA1535)	Not genotoxic in all strains	6
Ascophyllum Nodosum Extract	Not specified	150, 500, 1500, or 5000 µg/ml; in water	Mammalian cell gene mutation test accordance with OECD GL 476 (in vitro mammalian cell gene mutation test) with and without metabolic activation. Positive control without metabolic activation: ethylmethanesulphonate, with metabolic activation: BaP	CHO; K1 sub clone CHO K1	Increased mutant frequencies at 1500 and 5000 µg/ml without metabolic activation; no increase in mutation frequencies at lower concentrations. No increase in mutation frequencies at any concentration with metabolic activation.	6
Ascophyllum Nodosum Extract	Not specified	With metabolic activation: 0.63, 1.25, 2.5, or 5 mg/ml; without metabolic activation: 1.25, 2.5, or 5 mg/ml	Chromosome aberration assay in accordance with OECD GL 487 (in vitro mammalian chromosome aberration test) with and without metabolic activation. Negative control: medium (serum free cell culture medium); positive controls: CPA, MMC, and colchicine	Human lymphocytes	Not genotoxic	6
Ascophyllum Nodosum Extract	Not specified	Experiment I: With metabolic activation: 1.25, 2.5, or 5 mg/ml; without metabolic activation: 1.25, 2.5, or 5 mg/ml Experiment II: without metabolic activation: 0.63, 1.25, 2.5, or 5 mg/ml Serum free cell culture medium	Chromosome aberration assay in accordance with OECD 487 with and without metabolic activation. Negative control: solvent (serum free cell culture medium); Positive control: CPA, MMC, colchicine	Human peripheral lymphocytes	Not genotoxic or cytotoxic	6
Cystoseira Compressa Extract	n-Hexane, chloroform, and methanol	1, 2.5, or 5 mg/plate	Ames Assay with and without metabolic activation. Negative control: DMSO. Positive controls: BaP, 2-nitrofluorene, and sodium azide.	*S. typhimurium* (strains TA98 and TA100)	Not mutagenic	40
Ecklonia Cava Extract	Enzymatic extraction	911 - 3500 µg/plate; distilled water	Ames assay, with and without metabolic activation. OECD GL 471	*S. typhimurium* (strains TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2uvrA)	Not genotoxic	21

Table 23. Genotoxicity studies

Ingredient/Test Article	Extraction Solvent/ Method	Concentration/ Vehicle	Procedure	Test System	Results	Reference
Ecklonia Cava Extract	Alcohol	Up to 5000 µg/plate; vehicle not specified	Ames assay, with and without metabolic activation	*S. typhimurium* (strains TA98, TA100, TA1535, and TA1537) and *E. coli* (WP2uvrA(pKM101))	Not genotoxic or cytotoxic	[9]
Ecklonia Cava Extract	Alcohol	Up to 290 µg/mL	Chromosome aberration test, with and without metabolic activation	CHL cells	Not genotoxic	[9]
Ecklonia Cava Extract	Enzymatic extraction	87.5 – 350 µg/plate; distilled water	Chromosome aberration test, with and without metabolic activation. OECD GL 473	CHL cells	Not genotoxic	[21]
Fucus Vesiculosus Extract	Aqueous	0, 0.25, 0.5, or 1 mg/ml; cell medium	Chromosome aberration assay OECD GL 487	Human peripheral lymphocytes	Frequency of chromosome aberrations, mitotic index and extent of DNA damage in cells treated with extract were similar to controls at all concentrations.	[67]
Fucus Vesiculosus Extract	Aqueous	0, 0.25, 0.5, or 1 mg/ml; cell medium	Comet assay	Human peripheral lymphocytes	Extent of DNA damage in cells treated with extract was similar to controls at all concentrations.	[67]
			In Vivo			
Ecklonia Cava Extract	Alcohol	0 or 2000 mg/kg	Micronucleus assay. Test substance administered via oral gavage. Bone marrow (2,000 erythrocytes) was checked for frequency of micronuclei, after 24, 48, and 72 h.	Male Crlj:CD1(ICR) mice (n = 3)	There was no increase in frequency of micronuclei in any of the time points.	[9]
Ecklonia Cava Extract	Alcohol	0, 500, 1000, or 2000 mg/kg	Micronucleus assay. Test substance administered via oral gavage. Bone marrow (2,000 erythrocytes) was checked for the frequency of micronuclei, after 24 h.	Male Crlj:CD1(ICR) mice (n = 5)	There was no increase in frequency of micronuclei polychromatic erythrocytes (PCE)/(PCE + normochromatic erythrocytes (NCE)) ratio was not significantly different between treatment groups and control groups. No evidence of genotoxicity.	[9]
Ecklonia Cava Extract	Enzymatic extraction	1000, 2000, or 3000 mg/kg; distilled water	Mouse micronucleus assay. The number of mice used in the study was not provided. Administered by gavage. Saline and MMC were the controls. OECD GL 474	Male ICR mice	There were no mortalities or abnormal clinical signs in any group. There were no increases in structural or numerical chromosomal aberrations at any dose compared to the negative control.	[21]

BaP = benzo(a)pyrene; CHL = Chinese hamster lung; CHO = Chinese hamster ovary; CPA = cyclophosphamide; HCl = hydrochloric acid; MMC = mitomycin C; MNPCE = micronucleated polychromatic erythrocyte; NCE = normochromatic erythrocyte; PBS = phosphate-buffered saline; PCE = polychromatic erythrocytes

Table 24. **Tumor promotion studies**

Test Article	Extraction/solvent/ method	Dose/Exposure Route	Species (n)	Tumor Type	Carcinogenicity Model	Results	Reference
				Dermal			
Undaria Pinnatifida Extract	Dichloromethane extract	1 mg	Female ICR mice (n not specified)	Skin	- Initiation: a single dermal dose of DMBA (50 µg) - 1 week later, mice were dermally treated twice per week with TPA (1 µg) or Undaria Pinnatifida Extract (1 mg) 1 h prior to treatment with TPA for 15 weeks	TPA: tumors > 1 mm were observed after week 8; average number of tumors was 3.7. Undaria Pinnatifida Extract and TPA: mice did not show 1-mm tumors until week 14 (< 5%); average number of tumors was 0.2.	[70]
				Oral			
Hizikia Fusiforme Extract	95% Ethanol aq.	0, 2%, or 6% in feed	Male F344 rats (10, control, 8)	Colorectal	- Group 1 – standard diet - Group 2 – injected with AOM (15 mg/1 ml/kg once a week for 2 weeks) and standard diet - Group 3 – Injected with AOM and diet with 2% Hizikia Fusiforme Extract - Group 4 – Injected with AOM and diet with 6% Hizikia Fusiforme Extract - After 8 weeks, the rats were killed and necropsied.	- Body weights were similar among groups at 11 weeks. - No tumors were found in the negative control group and 58 tumors were found in the positive control group. Treatment groups had reduced number of tumors (21 each). - Immuno-histochemistry analysis of PCNA expression, a marker of tumor cell proliferation and apoptosis, was lower in treatment groups than in treated control group.	[71]
Saccharina Angustata Extract (inference from *Saccharina angustata* powder)	Dried and milled	0 or 5% in feed	Female Sprague-Dawley rats (54)	Mammary	- After 50 days on respective diets, 4 rats in each group were killed and examined for abnormalities. None were found. - At 55 days treatment groups were administered DMBA by gavage after fasting. - Rats were palpated weekly for tumors. - The rats were killed at 181 - 188 days after DMBA administration and necropsied.	- Weight gains were similar among groups. - First tumors in the control group appeared at 11.0 weeks and 19.8 in the treatment group. - 41 of 54 rats (76%) in control group and 34 of 54 rats (63%) in the treatment group had 1 or more adenocarcinomas at necropsy. - During treatment, 13 rats (8 control and 5 experimental) were euthanized between 74 and 170 days post- DMBA. 10 of these rats had developed large (~ 4 cm in diameter) mammary tumors, 2 developed malignant lymphomas, and 1 developed a large necrotic ear gland tumor (Zymbal's gland carcinoma). There were no other deaths. - 12 tumor-free rats (6 from each group) were found to have small nonpalpable mammary masses; 11 of these were found to be adenocarcinomas and 1 to be an adenoma. 93% of all tumors found in the mammary gland region at autopsy were adenocarcinomas; 5 tumors, which were mostly fibroadenoma but which had focal proliferations of malignant epithelial cells. Other tumors consisted of 7 fibroadenomas, 5 adenomas, 3 epidermal inclusion cysts, and 1 adenocarcinoma of sebaceous glands.	[72]
Sargassum Pallidum Extract	Aqueous. Boiled under reflux and filtered.	400, 600 or 800 mg/kg/day	Male Wistar rats (10)	Gastric	- Group 1 – distilled water - Group 2 – 800 mg/kg/day Sargassum Pallidum Extract - Group 3 - 6 – MNNG (25 mg/ml) in drinking for 25 weeks; then 0, 400, 600, or 800 mg/kg Sargassum Pallidum	- There were no mortalities. - Compared to group 1 (control), Sargassum Pallidum Extract increased serum IL-2, IL-4, and IL-10 levels in group 2; serum IL-2, IL-4, and IL-10 levels in group 3 were decreased. - Compared to group 1, Sargassum Pallidum Extract	[73]

Table 24. Tumor promotion studies

Test Article	Extraction/solvent/ method	Dose/Exposure Route	Species (n)	Tumor Type	Carcinogenicity Model	Results	Reference
					Extract for 8 weeks - All rats were killed at 33 weeks, blood analyzed, and stomachs examined.	decreased serum IL-6, IL-1β, and TNF-α levels in group 2; serum IL-6, IL-1β, and TNF-α levels in group 3 were increased. - Compared with group 3, Sargassum Pallidum Extract dose-dependently decreased serum IL-6, IL-1β, and TNF-α levels in groups 4, 5, and 6. - Concentration of serum and gastric mucosa MDA decreased in a dose-dependent manner in groups 4, 5, and 6. - Concentration of serum and gastric mucosa GSH and antioxidant enzyme activities increased in a dose-dependent manner in groups 4, 5, and 6. - Sargassum Pallidum Extract could decrease inflammatory response and improve immunity function partly through stimulating inflammatory cytokines (IL-2, IL-4, IL-10) production and inhibiting pro-inflammatory cytokines production.	
Undaria Pinnatifida Powder	Not specified	0, 1.0% or 5.0% in feed	Female Sprague-Dawley (SD) rats (11)	Mammary	- Initiation: a single dose of DMBA (20 mg) by gastric intubation - Once tumors reached 1 cm, rats were dived between 3 treatment groups for 8 weeks - Rats were then killed and all mammary tumors were histologically examined and thyroid glands, ovaries, and adrenal glands were weighed. Blood samples collected for measurement of serum total iodine concentration and serum T4 levels.	No differences in body weight gains between groups. Tumors in control group increased by more than 450%; tumor growth was suppressed in the 1% group and there was almost no change in tumor size in the 5% group. Mean combined weight of all mammary tumors of each rat in treatment groups was lower than that in the control group (~ 7 vs 20 g) at end of experiment. Weights of thyroid glands, ovaries, and adrenal glands did not differ among groups. Concentration of serum iodine was greater in treatment groups compared to controls. Serum iodine concentration had a positive relationship with concentration of Undaria Pinnatifida Powder in diet. Serum T4 levels showed no differences among groups. Test substance did not promote mammary tumors and suppressed tumor growth after a single dose of DMBA.	[74]
Undaria Pinnatifida Extract	Filtered aqueous extract of powdered stems and thick leaves (1.5 g in 1000 ml distilled water)	0 or 100% for water	Female Sprague-Dawley (SD) rats (12)	Mammary	- Initiation: a single dose of DMBA (20 mg) by gastric intubation - 1 week later, treatment began for 32 weeks - Mammary tumors were removed and measured	- Body weight gains were similar in both groups - Incidence of tumors at end of experiment was 22% vs 100% (controls) - The number of tumors was an average of < 1 vs. ~ 7 (controls) - Total tumor diameters was < 250 vs > 5000 mm - Histologically, mammary tumors were cystic adenocarcinoma, and tumors in treatment group had a decreased density of epithelial cells and fibrosis.	[66]

AOM = azoxymethane; DMBA = 7,12-dimethylbenz(*a*)anthracene; GSH = glutathione; MDA = malondialhehyde; MNNG = *N*-methyl-*N'*-nitro-N-nitrosoguanidine; PCNA = proliferating cell nuclear antigen; T4 = thyroxin; TPA = 12-*O*-tetradecanoylphorbol-13-acetate

Table 25. **Change in menstrual cycle with the oral administration of Fucus Vesiculosus Powder**[80]

	Menstrual cycle length			Days of Menstruation		
Subject	**Baseline**	**Low-Dose**	**High-Dose**	**Baseline**	**Low-Dose**	**High-Dose**
1	16.3 ± 0.6 days	26.0 ± 1.4 days	31.2 ± 1.1 days	9.3 ± 0.6 days	6.3 ± 1.8 days	4.5 ± 0.7 days
2	23.0 ± 1.7 days	28.5 ± 0.7 days	-	8.0 ± 1.0 days	5.3 ± 2.5 days	-
3	27.3 ± 0.6 days	31.5 ± 0.7 days	36.0 ± 2.8 days	6.3 ± 1.5 days	5.8 ± 0.4 days	3.5 ± 0.7 days

- = no data

Table 26. **Case Reports of brown algae**

Ingredient/substance (dose, if known)	Details	Reference
Fucus vesiculosus supplement (1200 mg 3 times per day)	18-year-old female presented with polyuria, polydipsia, extreme faintness, and a general poor condition. She had been on a hypocaloric diet for 3 months and taking *Fucus vesiculosus* supplements. Renal biopsy showed widespread tubular degeneration, and diffuse lymphomonocytic infiltrate; the glomeruli displayed scarce and focal mesangial proliferation, but the basal membrane appeared intact. The supplement was tested for heavy metals: arsenic, 21.3 mg/kg; cadmium, 0.3 ppm; mercury, 0.06 ppm; and chrome, 4 ppm. The patient recovered within 1 year.	[112]
Kelp tablets	54-year-old female developed thrombocytopenia with mucocutaneous bleeding after ingesting kelp tablets (that contained 1.3 µg/g arsenic) twice daily for 6 weeks. Marrow aspirate demonstrated normal megakaryocytes and dyserythropoiesis. After discontinuation of the supplements and treatment with steroids and azathioprine, her platelet count recovered after 3 months.	[113]
Kelp supplements	A 54-year-old woman presented with a 2-year history of worsening alopecia and memory loss. She also had a rash, increasing fatigue, nausea, and vomiting to the point of disablement. She took daily kelp supplements. A urine sample showed an arsenic level of 83.6 µg/g creatinine (normal < 50 µg/g creatinine). A sample from her kelp supplements contained 8.5 mg/kg arsenic. Within weeks of discontinuing the supplements, her symptoms resolved and arsenic blood and urine levels were undetectable.	[114]

Table 27. **Oral clinical trials**

Test Article	Extraction/ Solvent Method or Characterization	Study group	Study Details	Results	Reference
Ascophyllum Nodosum Powder (0.5 g/day)	Powdered plant	Healthy female subjects (n = 42)	After a 4-day period of keeping a food diary, subjects were administered capsules containing extract or potassium iodide daily for 14 days, then repeated 4-day food diary. All-day urine sample was collected on fourth day of run-in period and last day of treatment period (day 19) and fasted blood samples were collected on fourth day of run-in period and on day after treatment period (day 20).	There was an increase in urinary iodine concentrations (median 140 mg/l vs78 mg/l) in the treatment group. TSH increased slightly but within normal range 2 subjects. Increase in TSH concentrations may be associated with iodine-induced hypothyroidism, especially in those subjects with low iodine stores, although no change in the concentrations of thyroid hormones was observed. There were no adverse events reported during this experiment.	[78]
Ecklonia Cava Extract (400 mg/day)	Alcohol	Subjects with hyper-cholesterolaemia (n = 52)	Uncontrolled, open-label, single-arm study for 12 weeks	Hematological, clinical chemistry, and urinalysis did not reveal any adverse effects. There was one instance (2.2%) each of nausea, dyspepsia, diarrhea, and alopecia reported.	[9,79]
Ecklonia Cava Extract (0, 72, or 144 mg/day)	Phlorotannin-rich	Overweight subjects (n = 32 or 33)	Randomized, double-blind, three-arm, parallel trial for 12 weeks	Hematological and clinical chemistry did not reveal any adverse effects. Only high-dose group showed significant decreases in serum glucose and systolic blood pressure. No adverse signs were observed during the trial.	[9]
Ecklonia Cava Extract (0 or 400	Alcohol	Overweight subjects (n = 40)	Randomized, double-blind, and placebo-controlled trial for 12 weeks. Administered as 200 mg twice per	There were no adverse events reported that were related to the test substance.	[22]

Table 27. Oral clinical trials

Test Article	Extraction/ Solvent Method or Characterization	Study group	Study Details	Results	Reference
mg/day)			day in capsules		
Undaria Pinnatifida Powder (desalinated; 5040 mg/day)	Powdered	Hypertensive subjects (n = 18)	Subjects were gender and age matched to control group. Capsules (420 mg/capsule; 4 capsules/dose) 3 times/day with meals. Examined for body weight, BP, and blood chemistry parameters prior to experiment, at 4 weeks, and at 8 weeks. 1 subject in treatment group left study for personal reasons, so final number of paired subjects was 18, (some of her data (e.g., adverse effects) were used).	Compliance was not consistent; 6 subjects followed protocol; 1 ingested 9 capsules/day, 2 ingested 8 capsules/day, 6 ingested 6 capsules/day, and 3 ingested 3capsules/day. Average intake was estimated to be 7.9 capsules or 3.3 g/day. Average SBP in treatment group decreased by 13 mmHg from the baseline after 4 weeks, and was reduced by 8 mmHg below baseline after 8 weeks. Average DBP decreased by 9 mmHg from baseline after 4 weeks and by 8 mmHg after 8 weeks. There were no significant changes in either SBP or DBP in control group. However, the differences in reductions in SBP and DBP were significant between the treatment group and control group. Hypercholesterolemia subjects in treatment group had decreased total cholesterol by 8% after 4 weeks; no changes were observed in subjects with normal cholesterol levels. Adverse effects included 2 cases of indigestion and 1 case of diarrhea, all of which resolved quickly without treatment.	[42]

BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure; TSH = thyroid-stimulating hormone

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