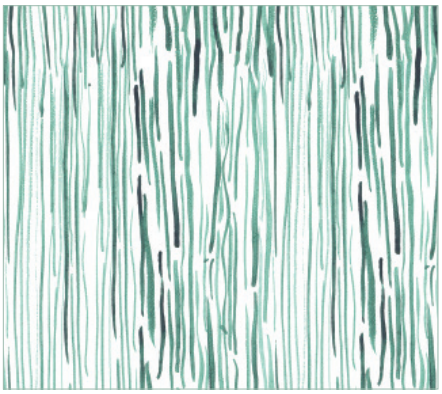

Clinical Studies of the Safety and Efficacy of Macroalgae Extracts in Cosmeceuticals

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ABSTRACT

BACKGROUND: There is a growing body of *in-vitro* and *in-vivo* laboratory research on the skin bioactive properties of macroalgae. **OBJECTIVE:** We sought to examine the scientific literature for evidence supporting the clinical safety and efficacy of macroalgae-derived ingredients in cosmeceuticals. **METHODS:** We performed a systematic review of scientific and medical electronic databases for published, peer-reviewed, randomized controlled trials and nonrandomized reports on the clinical bioactivity of topical macroalgae extracts in skin. **RESULTS:** Several human studies report scientific data supporting the safety and efficacy of macroalgae-based skincare products, focusing on skin-moisturizing, anti-melanogenic, and anti-cellulite (slimming) benefits. **CONCLUSIONS:** Further clinical research is necessary to determine the long-term safety, efficacy, optimal concentration and formulation of macroalgae extracts in cosmeceuticals with respect to previously reported and yet uninvestigated skin-directed potential functionally and bioactivity.

KEY WORDS: Macroalgae, seaweed, safety, efficacy, clinical trials

There is an increasing demand among consumers for naturally-derived ingredients, including macroalgae (i.e., seaweed) extracts, in skincare products, with demonstrated efficacy and safety.[1–5] Despite the growing popularity of seaweed-derived ingredients in cosmetic preparations, little has been reported to date regarding their specific bioactivity in human clinical studies. Over the past 20 years, there has been a growing body of *in-vitro* (bench) and *in-vivo* (animal) laboratory research on the skin bioactive properties of macroalgae, and many of these studies have focused on the potential for use of these diverse compounds as cosmeceutical ingredients.[1–5] While many ingredient suppliers and skincare brands promote the results of human cosmetic testing of macroalgae extracts on their websites and in company literature, there exists a relative paucity of peer-reviewed publications on this topic at this time.

The objective of this review was to examine the literary evidence supporting the clinical safety and efficacy of topically applied macroalgae-derived ingredients for cosmeceutical purposes.

METHODS

We performed a systematic search in October 2020 for peer-reviewed published clinical studies listed in the PubMed, Cochrane, EMBASE, and/or SCOPUS database. Search terms and keywords included "macroalgae," "algae," or "seaweed," combined with "cosmetic" or "cosmeceutical." Two reviewers independently screened articles based on inclusion criteria. Included articles were randomized controlled trials and nonrandomized reports. We examined the bibliographies of included articles and literature reviews to ensure that all relevant scientific reports were identified.

RESULTS

Studies that met inclusion criteria are summarized in Table 1. We identified eight human studies that evaluated the clinical safety and efficacy of macroalgae (i.e., seaweed) extracts in cosmeceuticals. Table 1 provides a detailed summary of identified studies, and highlights study designs, treatment parameters, results, adverse events, and mechanisms of action.

DISCUSSION

Macroalgae, or seaweeds, are aquatic, multicellular, and photosynthetic organisms that live in coastal, intertidal areas, in addition to freshwater locations, worldwide.[1–5] Approximately 15,000 species have been described, ranging in size from a few centimeters to over 100 meters in length, and are classified according to their pigmentary composition, nature of their cell walls, and reserve polysaccharides. Three groups exist: Phaeophyceae (brown), Rhodophyceae (red), and Chlorophyceae (green).[1–5] Macroalgae have simpler structures than terrestrial plants (lacking roots and conductive tissues, and capable of absorbing nutrients throughout their

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TABLE 1. Human studies evaluating clinical efficacy and safety of macroalgae extracts in cosmeceuticals

MACROALGAE	FORMULATION	APPLICATION	STUDY DESIGN	STUDY PARAMETERS	RESULTS	MECHANISM(S) OF ACTION	REFERENCE
Codium tomentosum	Moisturizing creams, with or without 5% macroalgae extract	One application; twice daily application for 7 days	10–12 women (aged 21–46 years), forearm skin, treated and untreated	Skin moisture (corneometer), zero minutes to six hours post-application; transitory thermal transfer (microeffusivimeter), days 0–8	2–3 times increased skin hydration with macroalgae extract compared with placebo	Hydration of all epidermal layers; protective barrier effect of sulphated phycocolloids; diffusion of osmoregulatory molecules	Mekideche et al.[6]
Laminaria japonica	12 Korean seaweed extracts, 5% (screening); and strongest moisturizing seaweed, 0%–15% vs. placebo	8-hr observation period, single application	10 women (aged 24–31 years), inner forearm, treated and untreated skin	Skin moisturizing activity, skin hydration, skin barrier function (TEWL), patch testing; corneometer and evaporimeter measurements	*Laminaria japonica* showed strongest moisturizing activity of 12 seaweed species tested. Dose-dependent increase in skin hydration with 0%–10% *L. japonica* extracts compared with untreated skin. Lowest TEWL seen with 10% *L. japonica*. Patch testing 100% negative	Humectant and hydrocolloid effects	Choi et a.[7]
Rhizoclonium hieroglyphicum	Creams, 0.3% aqueous extract vs. 5% glycerin vs. 5% propylene glycol vs. 0.5% hyaluronic acid vs. control	Short-term (< 1 hour) and long-term (1 week, twice daily)	30 Thai subjects, both male and female (aged 30–60 years), forearm skin (treated vs. untreated)	Short-term (15, 30, and 60 minutes) and long-term (1 week) moisturizing effects; corneometer; patient questionnaire	Macroalgae-based cream increased skin hydration after both short-term and long-term use. No skin irritation noted. More than 80% of subjects were satisfied with macroalgae-based cream	Humectant and occlusive effects. Skin moisturizing polysaccharides and amino acids.	Leelapornpisid et al.[8]
Fucus vesiculosus	1% aqueous extract vs. placebo	5 weeks, twice daily	10 women (aged 23–36 years), double-blind, split-face	Skin thickness (B-mode ultrasound); elastic properties (cutometer); twice daily measurements	Significant decrease (7-8%) in skin thickness and significant improvement in elasticity compared with controls. No irritation or erythema noted	Promotes contraction of fibroblast-populated collagen gels through increased expression of surface α2 and β1 integrins on human skin fibroblasts	Fujimura et al.[9]
Undaria pinnatifida (85% fucoidan), *Fucus vesiculosus* (60% fucoidan and 30% polyphenol)	0.3% gel extracts vs. placebo and control	Application before and/or after UV irradiation	25 Caucasian subjects, placebo-controlled	Skin erythema (mexameter); TEWL (tewameter)	Both extracts showed significant reduction in erythema and TEWL compared to placebo and control. *F. vesiculosus* extract exerted slightly superior results against UV damage	Fucoidan-rich extracts exert effects on genes, proteins and enzymes related to skin aging (SIRT1, elastase, collagenase), non-enzymatic glycation, and wound healing (Toll-like receptors)	Fitton et al.[10]
Fucus vesiculosus (60% fucoidan and 30% polyphenol)	0.3% gel extract vs. placebo	60 days, twice daily	20 Caucasian subjects, randomized, double-blind, placebo-controlled, split-face	Skin brightness (colorimeter); wrinkle depth (Primos 3D); age spot melanin index (mexameter)	50% showed an improvement in skin brightness, 65% showed a reduction in skin spot appearance, and 45% showed an improvement in the appearance of wrinkles	Free radical and tyrosinase inhibition. High polyphenol content may provide additional efficacy in antioxidant and skin brightening applications	Fitton et al.[10]
Ascophyllum nodosum and *Crithmum maritimum*	Natural ingredient regimens with 2 macroalgae extracts vs. 4% hydroquinone, 0.05% tretinoin	18 weeks (12-week treatment phase and 6-week nontreatment, regression phase); second 1-year open trial	56 women of 3 different races (aged 27–64 years), 3-armed parallel, investigator-blinded; 31 women in second trial, full face, open study	Hyperpigmentation (mottled HP, dyschromia and melasma); expert clinical grading, photography	Macroalgae and herbal blends have comparable efficacy in treating HP and preventing rebound mottled HP, dyschromia and melasma as commercial regimen. Continued visible improvement of HP with natural regimens without irritation or sensitization at 1 year	Inhibition of all but one (13 of 14) of the steps in melanin synthesis, activation and distribution; synergistic efficacy	Thornfeldt et al.[11]
Laminaria digitata, *Gelidium cartilagineum* and *Pelvetia canaliculata*	Topical product with 3 macroalgae extracts vs. placebo	4 weeks, once daily at night	90 women (aged 18–46 years), with fat accumulation on buttocks, thighs, waist and hips, randomized, double-blind	Clinical measurements of circumference; instrumental evaluation of skin thickness (ultrasound); self-evaluation	Significant decrease in waist/hip/thigh circumference and skin thickness with active product vs. placebo.	Adipolysis and microcirculation stimulation	Berardesca et al.[12]
Furcellaria lumbricalis and *Fucus vesiculosus*	Topical product with 2 macroalgae extracts vs. placebo	12 weeks, once daily	35 women (aged 36–65 years) with cellulite on thighs (grade: 3.5–5), randomized, double-blind, placebo-controlled	Clinical dermatological grading at 4, 8, and 12 weeks; ultrasound measurements (adipose tissue thickness)	Significant decrease in cellulite grade after 8 and 12 weeks vs. placebo. Significant decrease in fat thickness at 12 weeks vs. placebo. No adverse reactions	Dual mechanistic actions: stimulate lipolysis and increase pro-collagen I production	Al-Bader et al.[13]

TEWL, transepidermal water loss; UV, ultraviolet; HP, hyperpigmentation.

whole structure), but are known to contain 10 times greater amounts of diverse bioactive compounds.[1–5]

Macroalgae produce both primary metabolites, which are directly involved in normal physiological functions—namely, growth, development, and reproduction—and secondary metabolites, which are produced under different stress conditions, such as exposure to ultraviolet (UV) radiation, changes in temperature, nutrient availability, salinity or environmental pollutants.[1–5] Primary macroalgae metabolites include proteins, amino acids, polysaccharides, and fatty acids; the secondary metabolites produced include phenolic compounds, pigments, sterols, vitamins, and other bioactive compounds, allowing macroalgae to adapt and survive in varied and ever-changing environmental conditions. Each species of macroalgae expresses a unique set of primary and secondary metabolites.[1–5]

The diversity of macroalgae species and their widely ranging biochemical composition represent an important source of ingredients in skincare products (Table 2).[1–5] The importance of seaweed in the cosmetics industry is highlighted by the estimation that it makes up almost 40% of the world's hydrocolloid market. Macroalgae extracts can have one of three main functions in cosmeceutical formulations: (1) as additives that improve product stabilization, preservation, and/or organoleptic properties; (2) as excipients that constitute the transport medium for bioactive ingredients; and (3) as true functional compounds with cosmeceutical effects.[1–5]
A recent comprehensive review described potential cosmeceutical compounds derived from 103 macroalgae species, represented by 50 brown, 35 red, and 18 green seaweeds.[1] Cosmeceutical properties were classified into one of six bioactivities, including anti-aging (14%), antioxidant (39%), anti-inflammatory (14%), antimelanogenic (7%), anticancer (5%), and antimicrobial (21%).[1] Many macroalgae extracts have been reported to possess multiple biological functions.[1–5] The vast majority of this data are derived from *in-vitro* (bench) and *in-vivo* (animal) laboratory research.[1–5] In this review, we examined the peer-reviewed scientific literature for published clinical studies of safety and efficacy of macroalgae extracts in cosmeceuticals.

Mekideche et al.[6] evaluated the immediate and lasting skin moisturizing effects of *Codium tomentosum* (green seaweed). Using corneometry, they measured skin moisturization on the forearm skin of 10 women, at zero, three, 15, and 30 minutes and one, two, four, and six hours after a single application of creams with and without 5% *Codium* extract. The addition of macroalgae resulted in moisture levels remaining an average of 15% higher than in the control group after six hours compared to only 5% for creams without the seaweed active.[6] In the second part of this study, a microeffusivimeter was used to measure moisture levels in three layers of the epidermis (superficial, mid-, and deep) by transitory thermal transfer. Creams with and without 5% *Codium* extract were applied twice daily for seven days to the forearms of 12 women, with measurements taken at Days 0 to 8. The cream with *Codium* extract was reported to moisturize all epidermal layers.[6] The extract doubled moisture levels immediately after first application, remaining high for over three hours. Before application on Day 8, moisture levels in extract-treated skin were more than 20% higher than those in placebo-treated controls. The extract increased the moisturizing action of the placebo by 50% after application on Day 8. The authors concluded that the lasting and efficient hydration of all epidermal layers by *Codium* extract was due to the creation of a water "reservoir" via two mechanisms: (1) the formation of a protective barrier by attachment of extract-derived sulphated phycocolloids to skin proteins and (2) diffusion of osmoregulating molecules through the superficial epidermal layers, reinforcing the activity of the natural moisturizing factor (NMF) in the skin.[6]

Choi et al[7] screened 12 species of Korean seaweed (5% extracts) for skin moisturizing activity (using a corneometer) on treated (test vs. placebo cream) and untreated inner forearm skin in 10 women. After two hours, *Laminaria japonica* (brown seaweed) showed the strongest moisturizing activity among the screened seaweeds and was selected for further testing. There was a dose-dependent increase in skin hydration and a dose-dependent decrease in transepidermal water loss (TEWL) when using 0% to 10% *L. japonica* extracts compared with controls.[7] At two hours, hydration with 10% *L. japonica* extract increased by 14.44% compared to placebo (31.46% vs. 17.02%). For *L. japonica* extracts, improved hydration was maintained over the eight-hour observation period, with highest hydrating activity occurring at two hours. At eight hours, TEWL was decreased to 4.01 g/cm^2 with 10% *L. japonica* extract, which was approximately 20% of that seen with control. The authors postulated that *L. japonica* extracts hydrate skin via the humectants and hydrocolloids that this seaweed contains, making it a promising ingredient in moisturizing formulations.[7] Patch testing on human skin suggested that *L. japonica* extracts are safe to use at moderate doses. In addition, *L. japonica* extract did not affect the overall physicochemical characteristics or formulations of the test creams.[7]

Leelapornpisid et al.[8] evaluated the skin-moisturizing effect of *Rhizoclonium hieroglyphicum* (freshwater green macroalgae), compared to well-known commercial moisturizers, including glycerin, propylene glycol, and hyaluronic acid (HA), on human skin. In a clinical study of 30 healthy volunteers, skin hydration (measured by corneometry) increased after both short-term (less than hour) and long-term (one week) use of a 0.3% macroalgae extract–based cream compared to untreated skin. The short-term moisturizing effect of the 0.3% macroalgae cream was comparable to that of 0.5% HA cream ($P<0.05$).[8] The long-term skin hydration results for macroalgae cream were similar to those for glycerin, propylene glycol, and HA. More than 80% of study participants expressed satisfaction with the macroalgae cream. No skin irritation or allergic reactions were reported for the macroalgae extract. The authors suggested that the beneficial effects of this natural ingredient likely resulted from combined humectant and occlusive effects, in addition to the presence of high concentrations of skin-moisturizing polysaccharides (arabinose, rhamnose, xylose, and galactose) and amino acids (tryptophan, tyrosine, and phenylalanine).[8]

Fujimura et al.[9] investigated the effects of the topical application of an extract of *Fucus vesiculosus* (brown seaweed) on the thickness and mechanical properties of human skin. In cheek skin, the thickness normally increases and the elasticity usually decreases with age. A gel formulation that included 1% extract was applied topically to human cheek skin twice daily for five weeks. A significant decrease in skin thickness (~0.1 mm; ~7%–8%) measured by B-mode ultrasound was elicited ($P<0.005$), as was a significant improvement in elasticity measured with cutometry ($P<0.05$) as compared to in the control group.[9] No dose-dependency effect was identified—gels containing 2% to 5% macroalgae extract showed similar results

concerning skin thickness and elasticity as a 1% gel. These results suggest that 1% *F. vesiculosus* extract possesses significant anti-aging bioactivity and may be a useful ingredient in cosmeceutical formulations.[9]

Fitton et al.[10] used clinical (and *in-vitro*) studies to investigate two specific, well-characterized macroalgae extracts—with high concentrations of fucoidan and marine polyphenols—to assess their efficacy as topical cosmeceutical ingredients. These concentrated extracts were derived from the brown seaweeds *Undaria pinnatifida* (85% fucoidan) and *Fucus vesiculosus* (60% fucoidan and 30% polyphenol [polyphloroglucinol]). Clinical testing established the efficacy of both extracts in a range of tested applications.[10] Both extracts were proven to be clinically effective skin-soothing and skin-protecting agents, with significant reductions in erythema and TEWL following UV irradiation compared to the placebo and control groups ($P<0.05$). The *F. vesiculosus* extract exerted slightly superior clinical results compared to the *U. pinnatifida* extract.[10] *In-vitro* measurements found that the *F. vesiculosus* extract absorbed UV radiation in the skin-damaging UVA and UVB ranges, whereas the *U. pinnatifida* extract did not. Results from 20 subjects in a double-blind, placebo-controlled, split-face study showed that *F. vesiculosus* 0.3% extract was an effective cosmeceutical ingredient for clinically reducing the melanin index of age spots, increasing brightness, and decreasing wrinkles. Based on a dermatologist evaluation, after 60 days of use, 50% of study volunteers showed an improvement in skin brightness, 65% showed a reduction in skin spot appearance, and 45% showed an improvement in the appearance of wrinkles.[10] While the trial was terminated at 60 days, the rate of reduction in the age spot index and the increase in brightness exhibited marked trends. *In-vitro* testing demonstrated that the *F. vesiculosus* extract was a highly effective antioxidant and inhibitor of mushroom tyrosinase, unlike the *U. pinnatifida* extract. The improved antioxidant and clinical skin-brightening efficacy of the *F. vesiculosus* extract may be the result of its high polyphenol content.[10]

Thornfeldt et al.[11] evaluated a natural ingredient-based regimen (NI), consisting of two macroalgae-containing formulations with ingredients that not only inhibit tyrosinase, but modulate an additional 12 steps in the activation, synthesis, and distribution of the three types of melanin (pheomelanin, 5,6-dihydroxyindole-2-carboxylic acid eumelanin, and 5,6-dihydroxyindole eumelanin). The ingredients split between the two NI products included two macroalgae extracts (*Ascophyllum nodosum* and *Crithmum maritimum*), 22 herbal extracts, two naturally derived antioxidants, and three synthetic ingredients. When combined in these formulations, the ingredients in this regimen were expected to produce a synergistic efficacy. An initial trial consisted of 56 women of three different races (Caucasian [n=40], Hispanic [n=10], and Asian [n=6]) who were treated in a three-armed parallel, investigator-blinded prospective controlled clinical trial lasting 18 weeks.[11] The treatment phase was 12 weeks long, followed by a six-week, nontreatment regression phase. Three common types of hyperpigmentation (melasma, mottled hyperpigmentation, and diffuse dyschromia) were treated and compared with the results of a commonly prescribed regimen (4% hydroquinone and 0.05% tretinoin). The reduction in pigmentation was comparable between all the testing groups for full-face melasma, mottled hyperpigmentation, and dyschromia.[11] At no time point nor at any facial site in any of the three types of hyperpigmentation was the commercial regimen statistically superior to the macroalgae-containing regimen in efficacy parameters. A second one-year open trial of 31 patients of three different races documented continual visible improvement of hyperpigmentation with a lack of lesion rebound, and with no resistance, sensitization or irritation to continued therapy with the NI regimen that contained *A. nodosum* and *C. maritimum* extracts.[11]

Berardesca et al.[12] assessed the efficacy and tolerability of a topical, cosmeceutical treatment containing three macroalgae extracts and aimed at slimming fat deposits on the waist, hips, buttocks, and thighs of women. The macroalgae included two brown seaweeds (*Laminaria digitata* and *Pelvetia canaliculate*) and one red seaweed (*Gelidium cartilagineum*). The topical product was formulated using ingredients with two specific actions: adipolysis and microcirculation stimulation. The study involved 90 women, randomized to once-daily application at night for four weeks of active product (n=43) versus placebo (n=47).[12] The active product resulted in clinically significant improvements in all tested parameters of localized fat accumulation, such as skin and fat thickness reduction (as measured by ultrasonography) and circumference reduction, without a significant loss of weight.[12] The active product showed a mean circumference decrease of 2.1 cm for the waist, 1.8 cm for the hips, 2.3 cm for the upper thigh, and 1.8 cm for the thigh at the end of treatment, respectively. Uniform reduction of circumferences was noted, indicating a consistent response to therapy. The placebo did not result in any clinical slimming effect. Tolerability was good, and study subjects expressed full satisfaction with the active product under investigation.[12]

Al-Bader et al.[13] evaluated the clinical effects on cellulite of a cosmeceutical formulation containing *Furcellaria lumbricalis* (red seaweed) and *Fucus vesiculosus* (brown seaweed), combined with a retinoid, conjugated linoleic acid, and glaucine mixture. In a randomized, double-blind, placebo-controlled trial, 35 women with thigh cellulite applied the test product once daily for 12 weeks. There was a significant improvement in cellulite by dermatologist grading after eight and 12 weeks versus the placebo.[13] Ultrasound imaging showed a significant decrease in fat thickness compared with the placebo after 12 weeks. The authors proposed that a potent cocktail of ingredients, including macroalgae extracts, when combined together, can act synergistically to markedly enhance changes in cellulite. The macroalgae used (*F. lumbricalis* and *F. vesiculosus*) are believed to have the following dual mechanistic actions: (1) stimulating lipolysis, with an increase in free glycerol release, and (2) the capability of promoting pro-collagen I production, with effects on the surrounding extracellular matrix.[13]

The global cosmeceutical industry is increasingly turning to natural sources of bioactive-rich compounds, preferably from eco-friendly, abundant, renewable/sustainable, non-toxic and inexpensive raw materials.[1–5] The goal is to deliver innovative solutions that are believed to be "clean," "green," and "healthy"—meeting consumers' demands and expectations while providing satisfactory subjective results and positive objective outcomes.[1–5] Macroalgae are an excellent example of a natural resource that fits these requirements. The use of seaweed-derived ingredients in skincare products continues to grow, as scientific evidence largely from *in-vitro* and *in-vivo* studies supports their health-promoting, anti-aging, and other related cosmetic benefits in the skin.[1–5] This review paper highlights the results of several peer-reviewed human trials that confirm the safety, functional

activity, and clinical efficacy of macroalgae compounds in skincare products, with reference to skin-moisturizing, antimelanogenic, and anticellulite (slimming) benefits.[6–13] Several factors, including plant conditions (i.e., climate, habitat, time of year, plant health, portion of the plant used); harvesting conditions (i.e., harvesting time, transportation method, storage method and time); and processing conditions (i.e., timing and processing, extraction, and secondary purification methods) have been shown to influence the concentration of bioactives available in seaweed extracts.[1–5] Macroalgae-based cosmeceuticals are generally formulated using "whole plant extracts" with unknown quantities of bioactive ingredients rather than their purified compounds, which can make identification of the exact cause of their functionality difficult.[1–5] However, the use of crude macroalgae extracts allows for more cost-efficient manufacturing and may provide enhanced bioactivity in the skin as a result of synergistic effects of diverse compounds present that act on different pathways of skin-aging and other cutaneous cosmetic processes.[1–5]

TABLE 2. List of skincare brands with macroalgae-based products

SKINCARE BRAND	PRODUCT	WEBSITE LINKS
si SKIN Organics	Luminous Brightening Elixir	https://siskinorganics.com
	Spot-Less Pigment Corrector	
Le Mer	Intensive Revitalizing Mask	https://www.cremedelamer.com
	Lifting and Firming Mask	
Osea Malibu	Undaria Algae Body Oil	https://oseamalibu.com
	Undaria Body Polish	
Skinceuticals	Daily Moisture	https://www.skinceuticals.com
	Emollience	
PeterThomasRoth	Mega-Rich Intensive Anti-Aging Cellular Crème	https://www.peterthomasroth.com
	Irish Moor Mud Mask	
UNA	Day Cream	http://www.unaskincare.com
	Ultra Rich Eye Cream	
AMA Sea Beauty	DeepSea Serum	https://www.amaseabeauty.com
	SeaScrub	
Repêchage	Opti-Firm Renewal Complex Night Cream	https://www.repechage.com
	Mineral Face Shield	
VOYA	Pearlesque Hydrating Moisturiser	https://www.voya.ie
	Maskerade Soothing Facial Mask	

CONCLUSION

Macroalgae-derived compounds are natural, renewable cosmeceutical ingredients that can be easily and cost-effectively extracted. As a result of their abundance, chemical diversity, biocompatibility, desirable bioactivities, and physical properties, seaweed extracts are ideal for the development of safe and effective skincare products. Clinical studies to date demonstrate the skin-moisturizing, antimelanogenic, and anticellulite (slimming) benefits of topical macroalgae extracts. Further clinical research is needed to determine the long-term safety, efficacy, and optimal concentration and formulation of macroalgae-based cosmeceuticals with respect to previously reported and yet uninvestigated skin-directed potential functionally and bioactivity.

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