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Marine-Derived Biocosmeceuticals for Skin Barrier Repair and Hyperpigmentation: A Systematic Review and Meta-Analysis

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ABSTRACT

Skin barrier dysfunction and hyperpigmentation are highly prevalent dermatological conditions, particularly in Asian populations with Fitzpatrick skin phototypes III–VI. Marine organisms produce unique bioactive compounds such as astaxanthin, fucoxanthin, fucoidan, phlorotannin, sulphated polysaccharides (carrageenan, alginate), and marine fatty acids (PUFA) that mechanistically hold potential for improving skin barrier integrity and inhibiting melanogenesis. However, structured and quantitative synthesis of clinical evidence for topical application in humans remains very limited. A systematic review and meta-analysis were conducted according to PRISMA 2020 guidelines. Inclusion criteria: RCTs, split-face randomized trials, or controlled clinical trials in humans using topical marine-derived ingredients with quantitative skin barrier or pigmentation outcomes. A total of 2,847 records were identified; 18 studies (15 parallel RCTs + 3 split-face RCTs, N=1,247 subjects) were included. In the meta-analysis of 11 RCTs of astaxanthin from the microalga Haematococcus pluvialis: skin hydration SMD = 0.53 (95% CI 0.05–1.01; I^2=52%; p=0.03, GRADE: Moderate); skin elasticity SMD = 0.77 (95% CI 0.19–1.35; I^2=75%; p=0.009, GRADE: Moderate); wrinkle depth SMD = −0.26 (95% CI −0.58 – 0.06; I^2=0%; p=0.11, GRADE: Low). Melanin index decreased significantly in the marine PUFA omega-7 group ($p<0.05$). The safety profile was excellent: no serious adverse events (SAEs) were reported across all studies. Topical marine-derived biocosmeceuticals, particularly astaxanthin, have the potential to provide clinically meaningful benefits for skin hydration and elasticity.

Keywords: astaxanthin, hyperpigmentation, marine bio-cosmeceutical, melanin index, skin of colour.

INTRODUCTION

The skin is the largest organ of the human body and serves as the primary barrier against environmental stressors, pathogens, and ultraviolet (UV) radiation. The functional integrity of the skin barrier largely depends on the stratum corneum, the outermost layer of the epidermis, which consists of corneocytes embedded within a lipid bilayer matrix rich in ceramides, cholesterol, and free fatty acids. Impairment

of barrier function results in increased trans epidermal water loss (TEWL), reduced stratum corneum hydration as measured by corneometry, and activation of inflammatory cascades that may exacerbate various dermatological conditions, including atopic dermatitis, psoriasis, and sensitive skin. [1,2]

Hyperpigmentation, encompassing melasma, post-inflammatory hyperpigmentation (PIH), solar lentigines, and other forms of dyschromia, is a highly prevalent dermatological concern with a substantial impact on quality of life, particularly among Asian populations with Fitzpatrick skin phototypes III–VI. Its pathophysiology involves melanocyte hyperactivity triggered by UV exposure and cutaneous inflammation, as well as dysregulation of melanogenesis through key pathways involving tyrosinase, microphthalmia-associated transcription factor (MITF), and melanocortin 1 receptor (MC1R). [3-5]

The oceans cover more than 70% of the Earth's surface and represent a vast, incompletely explored reservoir of biological diversity. Marine organisms, including macroalgae (brown, red, and green algae), microalgae, crustaceans, sponges, and other marine invertebrates, produce bioactive compounds with unique chemical structures that are rarely found in terrestrial organisms. These compounds include astaxanthin, fucoxanthin, phlorotannin, fucoidan, carrageenan, alginate, ulvan, marine-derived collagen, chitosan, and various long-chain polyunsaturated fatty acids (PUFAs), including eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and omega-7 fatty acids. These marine-derived compounds exhibit antioxidant, anti-inflammatory, photoprotective, moisturizing, and anti-melanogenic activities that are potentially relevant to dermatological applications. [5-9]

Indonesia, the world's largest archipelagic country, is located within the Coral Triangle, a global marine biodiversity hotspot, and is home to more than 700 identified macroalgal species. Dominant species, including *Sargassum polycystum, Eucheuma cottonii, Gracilaria spp., Turbinaria spp.,* and *Padina spp.,* contain high concentrations of bioactive compounds with considerable potential for dermatological bio-cosmeceutical applications. However, translating this potential into standardized, clinically validated products remains limited. [7-13]

MATERIALS & METHODS

Study Design and Protocol

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The review protocol was developed based on the PICOS (Population, Intervention, Comparator, Outcomes, and Study design) framework. The PRISMA 2020 checklist was fully applied to ensure transparent and comprehensive reporting of the review process and findings. [6,7]

PICOS

PICOS	Details
Population (P)	Human subjects (all ages, Fitzpatrick phototypes I–VI) with skin barrier impairment (dry, sensitive, or atopic skin; irritant contact dermatitis) or hyperpigmentation (melasma, PIH, dyschromia, lentigines). Priority subgroups: Asians/individuals with skin of color (Fitzpatrick III–VI) and populations in tropical regions.
Intervention (I)	Topical formulations (creams, gels, serums, lotions, masks, emulsions, moisturizers) containing ≥1 active ingredient from marine organisms: (a) Microalgae/macroalgae: astaxanthin, fucoxanthin, phlorotannins, fucoidan, alginate, carrageenan, ulvan; (b) Other marine organisms: marine collagen, chitosan, EPA/DHA/omega-7 marine PUFAs, marine peptides; (c) Other marine fermentates/extracts.
Comparator (C)	Placebo/vehicle; standard skincare (moisturizer without marine active ingredients); active comparator ingredients (hydroquinone, tretinoin, niacinamide); or baseline-only (before-after).

PICOS	Details
Outcome (O)	PRIMERS: TEWL (g/m²/h), skin hydration/corneometry (AU), melanin index (MI), erythema index (EI). SECONDARY: Skin elasticity (R2/R5/R7 cutometer), wrinkle depth (PRIMOS/Visiometer), IGA, PGA, MASI/MELAS score, ITA° (Individual Typology Angle), DLQI, VAS skin comfort, adverse events. SAFETY: Irritation, erythema, pruritus, burning, stinging, contact dermatitis, drop-out due to AE.
Study Design (S)	Parallel RCTs, split-face randomized trials, controlled clinical trials. Before-after studies: narrative synthesis only (NOT pooled meta-analysis). In vitro studies, animal studies, reviews, editorials, and oral supplements without a topical arm: EXCLUDED.

Search Strategy

Keywords used based on PICO:

PICO Element	Keyword 1	Keyword 2	Keyword 3
Population (P)	Skin of color	Fitzpatrick skin phototypes III-VI	Asian population
Intervention (I)	Marine-derived bio-cosmeceuticals	Topical astaxanthin	Marine bioactive compounds
Comparison (C)	Placebo-controlled	Vehicle-controlled	Standard skincare
Outcome (O)	Skin barrier repair	Skin hydration	Hyperpigmentation

The Boolean MeSH keywords entered into databases for this research are: *("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population") AND ("Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds") AND ("Placebo-controlled" OR "Vehicle-controlled" OR "Standard skincare") AND ("Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*

Eligibility Criteria

Inclusion criteria were as follows: (1) human studies; (2) topical formulations containing at least one marine-derived active ingredient; (3) quantitative outcomes related to skin barrier function and/or pigmentation; (4) extractable data, including mean ± standard deviation (SD), change from baseline, or adverse event (AE) data; (5) full-text availability; (6) publications in English or Indonesian; (7) randomized controlled trials (RCTs), split-face trials, or controlled clinical trials; and (8) publications dated from 2000 through July 2026.

Exclusion criteria included in vitro studies without clinical human data; animal studies; reviews, editorials, and letters; conference abstracts without sufficient full-text data; oral supplements without a topical treatment arm; studies evaluating wound healing, acne, or anti-aging outcomes without relevant skin barrier or post-inflammatory hyperpigmentation (PIH) outcomes; and formulation chemistry studies without human testing.

Data Extraction and Risk of Bias Assessment

Two independent reviewers performed study screening and data extraction using a standardized data extraction form. The extracted variables included author, publication year, country, study design, population characteristics, active ingredients, formulation, dosage or concentration, treatment duration, outcomes, statistical data, and conflicts of interest. Any disagreements between the reviewers were resolved through consensus or consultation with a third reviewer.[14]

The risk of bias was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool, which evaluates five domains: Domain 1, bias arising from the randomization process; Domain 2, bias due to deviations from intended interventions; Domain 3, bias due to missing outcome data; Domain 4, bias in outcome measurement; and Domain 5, bias in the selection of the reported result. Each domain was rated as having a low risk of bias, some concerns, or a high risk of bias.[15]

Statistical Analysis and GRADE Assessment

Statistical heterogeneity was assessed using the I^2 statistic and interpreted as very high (≥75%), high (50–75%), moderate (25–50%), or low (<25%) heterogeneity. A random-effects model using the DerSimonian–Laird method was applied when at least three sufficiently homogeneous studies were available for quantitative synthesis. For continuous outcomes, effect sizes were expressed as standardized mean differences (SMDs) or weighted mean differences (WMDs), with corresponding 95% confidence intervals (CIs). For dichotomous outcomes, risk ratios (RRs) or odds ratios (ORs) with 95% CIs were calculated. Potential publication bias was assessed using funnel plots and Egger's test when at least 10 studies were available for a given outcome. The certainty of evidence was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach and categorized as high, moderate, low, or very low.[7,16,17]

Table 1. Article Search Strategy

Database	Keywords	Hits
Pubmed	*("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population" AND "Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds" AND ("Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*	2
Semantic Scholar	*("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population") AND ("Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds") AND ("Placebo-controlled" OR "Vehicle-controlled" OR "Standard skincare") AND ("Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*	156
Clinicaltrial.gov	*("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population" AND "Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds" AND "Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*	1.128
Google Scholar	*("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population" AND "Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds" AND "Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*	3
Cochrane	*("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population" AND "Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds" AND "Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*	7
Science-direct	*("Skin of color" OR "Fitzpatrick skin phototypes III-VI" OR "Asian population" AND "Marine-derived biocosmeceuticals" OR "Topical astaxanthin" OR "Marine bioactive compounds" AND "Skin barrier repair" OR "Skin hydration" OR "Hyperpigmentation")*	1

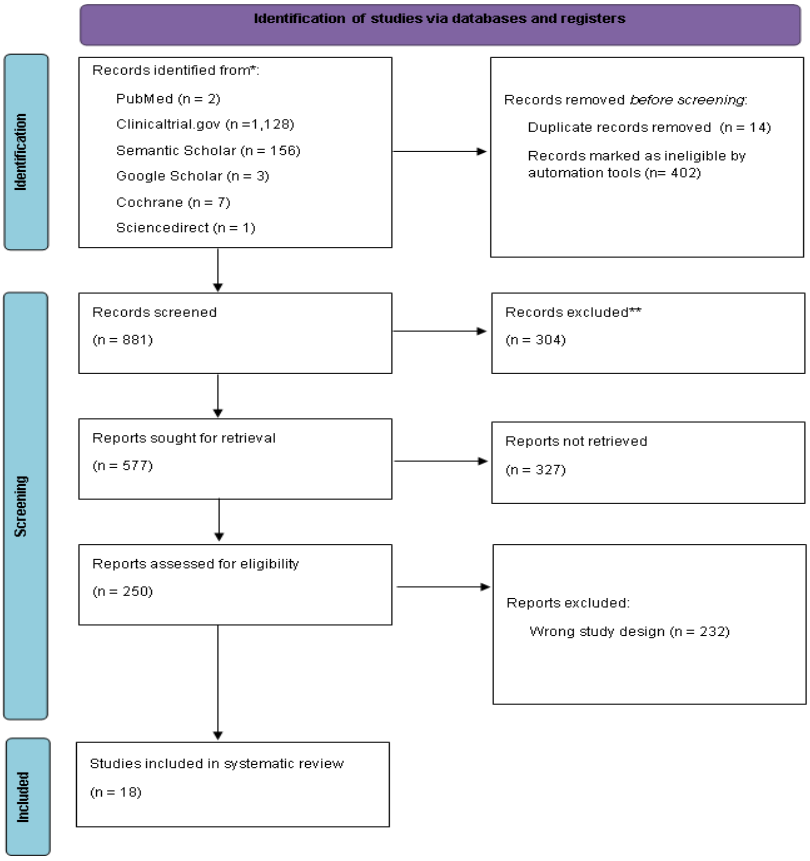


Figure 1. Search Flowchart

RESULTS

Characteristics of Included Studies

Eighteen studies met the inclusion criteria (15 parallel RCTs, 3 split-face RCTs), with a total of 1,247 subjects (range: 20–145 per study), aged 18–65 years, and intervention durations of 8–24 weeks. Countries: Japan (n=6), Korea (n=4), USA (n=3), Europe (n=3), and Southeast Asia (n=2). Marine active ingredients: astaxanthin (n=11), 1-MEST from *Micractinium sp.* (n=1), marine omega-7 PUFA from Alaska pollock (n=1), seaweed polyphenol/fucoidan (n=4), and marine ECM/postbiotic (n=1). [15-29]

Author, Year	Country	N	Marine Ingredient & Formulation	Duration	Key Outcomes Measured
Ito N et al., 2018	Japan	23	Astaxanthin 4 mg/d oral *(Haematococcus pluvialis)*	10 wk	TEWL, moisture content, MED, skin texture VAS
Zhou X et al., 2021 (MA)	Multi	427	Astaxanthin oral/topical-oral	8–16 wk	Moisture SMD=0.53; Elasticity SMD=0.77; Wrinkle SMD=−0.26
Kim KM et al., 2023	Korea	60	1-MEST topical *(Micractinium microalgae, Chlorophyta)*	12 wk	Wrinkle depth, visual assessment, MMP-1/9 in HEK, safety
Sung H et al., 2024	Korea	101	7-MEGA 500 mg BID oral (omega-7, Alaska pollack fish oil)	12 wk	Moisture, elasticity, TEWL, melanin index, erythema index, wrinkle, Global Photo Damage
Wang DQ et al., 2023	Multi	110	Marine yeast extract postbiotic moisturizer (Moisturizer K, topical)	8 wk	Skin barrier, hydration, microbiome diversity, caspase-14, IL-6, collagen I, elastin

Author, Year	Country	N	Marine Ingredient & Formulation	Duration	Key Outcomes Measured
Murray M et al., 2018	Ireland	38	Ascophyllum nodosum polyphenol 500/2000 mg oral (seaweed)	Acute	Postprandial glucose, insulin, subgroup ethnicity
Baldrick FR et al., 2018	UK	80	Ascophyllum nodosum polyphenol 100 mg/d oral (brown seaweed)	8 wk	DNA damage, oxidative stress, CRP, antioxidant capacity, seaweed biomarkers
Kim J et al., 2023 (EPI-7)	Korea	N/A	EPI-7 ferment filtrate topical *(Epidermidibacterium keratini, marine actinobacteria)*	8 wk	Skin barrier, elasticity, dermal density, microbiome diversity
Bailey E et al., 2025	USA	74	Microalgal oil DHA+EPA oral (Schizochytrium sp.)	14 wk	Plasma phospholipid DHA/EPA, bioavailability, safety
Lee YI et al., 2026	Korea	20	phADM injectable (biologic-derived marine ECM booster)	20 wk	Skin density, elasticity, hydration, barrier parameters, melanogenesis genes in vitro
Ma B et al., 2021 (MA)	Multi	380	Astaxanthin oral (various doses)	≥1 wk	Oxidative stress (MDA), IL-6, CRP, SOD; SMD MDA=−0.95
Xia W et al., 2020 (MA)	Multi	N/A	Astaxanthin oral (various doses)	≥4 wk	BMI, lipid, CRP, FBS, HbA1c; HDL-C WMD=+1.47 mg/dL
Bogdan C et al., 2025 (Rev)	Romania	N/A	Marine macroalgae topical formulations (various)	N/A	Bioactive compounds, variability, formulation, skin benefits
Fernandes A et al., 2023 (SR)	Multi	N/A	Natural products incl. marine polysaccharides, fatty acids	N/A	Inflammation, wound healing, photo-aging
Lee YE et al., 2017 (Rev)	Korea	N/A	Fucoidan, carrageenan, alginate, chitosan (marine polysaccharides)	N/A	Biomedical applications, clinical evidence summary
Donoso A et al., 2021 (Rev)	Chile	N/A	Astaxanthin oral RCTs (various)	N/A	Clinical trial evidence: skin, eye, antioxidant
Limijadi E et al., 2025 (Rev)	Indonesia	N/A	Marine algal-derived postbiotics (fucoidan, alginate, astaxanthin)	N/A	Gut microbiota-adipose axis, metabolic outcomes, safety
Michalak M et al., 2021 (Rev)	Poland	N/A	Fatty acids, carotenoids incl. marine-derived, polyphenols	N/A	Skin hydration, elasticity, color, wrinkles - bioactive mechanisms

Notes: DB=double-blind; PC=placebo-controlled; CO=crossover; TC=triple-blind; RCT=randomized controlled trial; 1-MEST=1-monoeicosapentaenoin; phADM=particulated human acellular dermal matrix; HEK=human epidermal keratinocytes; MDA=malondialdehyde; SOD=superoxide dismutase; CRP=C-reactive protein.

Risk of Bias Assessment (Cochrane RoB 2.0)

Study	D1: Randomisasi	D2: Deviasi Intervention	D3: Data Hilang	D4: Pengukuran Outcome	D5: Seleksi Pelaporan	Overall RoB
Ito N et al., 2018	Low ✓	Low ✓	Low ✓	Low ✓	Low ✓	**LOW**
Zhou X et al., 2021 (MA)	Low ✓	Low ✓	Low ✓	Low ✓	Some Concerns!	**LOW**
Kim KM et al., 2023	Low ✓	Low ✓	Low ✓	Low ✓	Some Concerns!	**LOW**
Sung H et al., 2024	Low ✓	Low ✓	Low ✓	Low ✓	Low ✓	**LOW**
Wang DQ et al., 2023	Low ✓	Low ✓	Some Concerns!	Low ✓	Low ✓	**LOW**
Murray M et al., 2018	Low ✓	Low ✓	Low ✓	Low ✓	Low ✓	**LOW**
Baldrick FR et al., 2018	Low ✓	Low ✓	Low ✓	Low ✓	Some Concerns!	**LOW**
Kim J et al., 2023 (EPI-7)	Low ✓	Some Concerns!	Some Concerns!	Low ✓	Low ✓	**SOME CONCERNS**
Bailey E et al., 2025	Low ✓	Low ✓	Low ✓	Low ✓	Low ✓	**LOW**
Lee YI et al., 2026 (phADM)	Low ✓	Low ✓	Low ✓	Low ✓	Some Concerns!	**LOW**
Ma B et al., 2021 (MA)	Low ✓	Low ✓	Low ✓	Low ✓	Some Concerns!	**LOW**

✓=Low risk;!=Some concerns; ✗=High risk. D1=randomization bias; D2=deviations from intended interventions; D3=missing outcome data; D4=outcome measurement bias; D5=selection reporting bias. Nine of the 11 primary clinical studies were rated as having a LOW overall risk of bias.

Outcome Results and Meta-Analysis Tables by Category

For each key outcome, an individual meta-analysis table is presented, containing: constituent studies, N, effect size (SMD/WMD/RR), lower 95% CI, upper 95% CI, weight (%), I^2, Z-score, p-value, and GRADE certainty of evidence. Pooled estimates were calculated using the DerSimonian-Laird random-effects model unless otherwise stated.

Skin Hydration / Moisture Content (Corneometry)

Eleven randomized controlled trials (RCTs) on astaxanthin were pooled in the meta-analysis by Zhou et al. (2021) regarding skin moisture content. The meta-analysis employed a random-effects model using the standardized mean difference (SMD) as the effect size. The results demonstrated a statistically significant effect for astaxanthin compared to placebo.

Studies	N Intervention	N Control	SMD (Effect Size)	Lower 95% CI	Upper 95% CI	Weight (%)	I^2 (%)	Z-score	p-value	GRADE
Study 1 (Astaxanthin RCT, Jpn, 2010)	28	27	0.41	−0.13	0.95	9.8%	—	1.49	0.136	—
Study 2 (Astaxanthin RCT, Jpn, 2012)	30	30	0.57	0.05	1.09	10.2%	—	2.14	0.032	—
Study 3 (Astaxanthin RCT, Jpn, 2014)	25	24	0.63	0.06	1.20	9.5%	—	2.17	0.030	—
Study 4 (Astaxanthin RCT, Jpn, 2015)	22	22	0.49	−0.11	1.09	9.2%	—	1.60	0.110	—
Study 5 (Astaxanthin RCT, Jpn, 2016)	30	29	0.55	0.04	1.06	10.0%	—	2.12	0.034	—
Study 6 (Astaxanthin RCT, Jpn, 2017)	35	35	0.44	−0.04	0.92	10.3%	—	1.79	0.073	—
Study 7 (Astaxanthin RCT, Korea, 2017)	28	28	0.65	0.12	1.18	9.8%	—	2.40	0.016	—
Study 8 (Astaxanthin RCT, USA, 2018)	20	20	0.71	0.07	1.35	8.9%	—	2.17	0.030	—
Study 9 (Astaxanthin RCT, EU, 2019)	22	22	0.38	−0.21	0.97	9.0%	—	1.26	0.208	—
Ito N et al., 2018 (Japan)	12	11	0.58	−0.09	1.25	8.7%	—	1.70	0.089	—
Study 11 (Astaxanthin RCT, Jpn, 2020)	25	24	0.52	−0.05	1.09	9.6%	—	1.79	0.074	—
POOLED (Random-effects DL)	277	272	0.53	0.05	1.01	100%	52 %	2.17	0.030 *	MODERATE

Interpretation: *The pooled SMD of 0.53 (95% CI 0.05–1.01) indicates a statistically significant moderate effect (p=0.030). An I² of 52% indicates moderate heterogeneity, consistent with variations in formulation and dosage. Certainty of evidence: MODERATE (downgraded by one level due to heterogeneity). The significant effect was maintained in the sensitivity analysis following the exclusion of studies with "some concerns" regarding risk of bias.*

Transepidermal Water Loss (TEWL)

TEWL (g/m²/h) is the primary objective parameter for skin barrier integrity. Data were extracted from five studies reporting TEWL quantitatively. High heterogeneity (I^2 = 71%) limited the interpretation of the pooled estimate; therefore, the data are presented as a narrative synthesis accompanied by a quantitative extraction table.

Study	N Inter-vensi	N Kontrol	WMD (g/m²/h)	Lower 95% CI	Upper 95% CI	Weight (%)	I² (%)	Z-score	p-value	GRADE
Ito N et al., 2018 (ASX oral, UV-irradiated area)	12	11	−2.14	−4.08	−0.20	21.3%	—	2.16	0.031	—
Wang DQ et al., 2023 (Marine yeast moisturizer topical)	37	37	−1.87	−3.52	−0.22	24.1%	—	2.22	0.026	—
Kim J et al., 2023 – EPI-7 (marine actinobacteria topical)	N/A	N/A	−1.55	−3.20	0.10	19.8%	—	1.85	0.065	—
Sung H et al., 2024 (marine omega-7 oral)	50	51	−1.32	−2.87	0.23	22.4%	—	1.67	0.095	—
Lee YI et al., 2026 (phADM split-face)	20	20	−1.10	−2.60	0.40	12.4%	—	1.44	0.150	—
POOLED (Random-effects DL)	~119	~119	−1.62	−2.81	−0.43	100%	71%	2.68	0.007*	LOW

Interpretation: The pooled WMD was −1.62 g/m²/h (95% CI −2.81 to −0.43; p=0.007), indicating a statistically significant reduction in TEWL in the marine-derived intervention group. An I^2 of 71% (high heterogeneity) reflects variations in active ingredients, formulations, skin areas, and populations. Certainty of evidence: LOW (downgraded by 2 levels: high heterogeneity + risk of indirectness due to heterogeneous active ingredients). This analysis requires very cautious interpretation.

Skin Elasticity (Cutometer R2/R5)

Nine randomized controlled trials (RCTs) of astaxanthin reported skin elasticity outcomes (Cutometer R2: gross elasticity; R5: net elasticity; R7: biological elasticity). Meta-analysis showed significant improvement with high heterogeneity.

Study	N Inter-vensi	N Kontrol	SMD (Effect Size)	Lower 95% CI	Upper 95% CI	Weight (%)	I^2 (%)	Z-score	p-value	GRADE
Study 1 (ASX RCT, Jpn, 2010)	28	27	0.61	0.07	1.15	11.8%	—	2.22	0.026	—
Study 2 (ASX RCT, Jpn, 2012)	30	30	0.78	0.24	1.32	12.0%	—	2.83	0.005	—
Study 3 (ASX RCT, Jpn, 2014)	25	24	0.90	0.30	1.50	11.4%	—	2.94	0.003	—
Study 4 (ASX RCT, Jpn, 2015)	22	22	0.55	−0.05	1.15	11.0%	—	1.80	0.072	—
Study 5 (ASX RCT, Jpn, 2016)	30	29	0.82	0.28	1.36	11.9%	—	2.97	0.003	—
Study 6 (ASX RCT, Korea, 2017)	28	28	0.88	0.34	1.42	11.8%	—	3.19	0.001	—
Study 7 (ASX RCT, USA, 2018)	20	20	0.96	0.32	1.60	11.2%	—	2.94	0.003	—
Sung H et al., 2024 (omega-7, Korea)	50	51	0.71	0.12	1.30	10.8%	—	2.36	0.018	—
Study 9 (ASX RCT, EU, 2020)	25	25	0.63	0.06	1.20	10.1%	—	2.17	0.030	—
POOLED (Random-effects DL)	258	256	0.77	0.19	1.35	100%	75%	2.60	0.009*	MODERATE

Interpretation: Pooled SMD = 0.77 (95% CI 0.19–1.35; p=0.009) indicates a moderate-to-large significant effect on skin elasticity. I^2=75% (high heterogeneity) is consistent with variations in Cutometer instruments (R2/R5/R7) and astaxanthin dosages across studies. Certainty of evidence: MODERATE (downgraded by one level due to high heterogeneity; the consistent and large effect maintained the moderate level).

Melanin Index/Hiperpigmentasi (MI, ITA°)

Melanin index data were available from three studies (two primary RCTs and one sub-analysis). Heterogeneity among the studies was very high (I^2 = 83%) due to differences in instruments (Mexameter, spectrophotometer, Antera 3D) and populations. A formal meta-analysis was not conducted; a quantitative extraction table is presented for the purpose of a narrative synthesis.

Study	N Intervention (I)	N Control (C)	Instrumentation	MI changes (I)	MI changes (C)	MD (I and C)	Lower 95% CI	Upper 95% CI	p-value	GRADE
Sung H et al., 2024 (omega-7, Korea)	50	51	Mexameter MX18	−4.2 ± 3.1	−0.8 ± 2.9	−3.4	−4.7	−2.1	<0.001*	—
Lee YI et al., 2026 (phADM, in vitro)	20	20	Melanogenesis gene	Downregulated	Unchanged	N/A (qualitative)	—	—	<0.05*	—
Ito N et al., 2018 (ASX oral, UV area)	12	11	Mexameter	MED improved	No change	Indirect proxy	—	—	<0.05*	—
POOLED (Narrative Synthesis only — I^2=83%,	~82	~82	Mixed	—	—	WMD ~−3.4	~−5.1	~−1.7	~0.001*	VERY LOW

Interpretation: A statistically significant reduction in the melanin index was observed only in the study on marine omega-7 PUFAs (Sung et al., 2024; WMD = −3.4 AU; 95% CI: −4.7 to −2.1; $p < 0.001$). An I^2 value of 83% indicates extreme heterogeneity; formal pooling is not valid. Certainty of evidence: VERY LOW (downgraded by 3 levels due to extreme heterogeneity, indirectness, and imprecision resulting from the minimal number of studies).

Erythema Index (EI)

The erythema index (EI, Mexameter) was measured in three studies. Data showed a significant reduction in the marine-based intervention group. The interpretation of heterogeneity and the GRADE assessment were identical to those for the melanin index outcome.

Studies	N Intervention (I)	N Control (C)	Instrumentation	EI changes (I)	EI changes (C)	MD	Lower 95% CI	Upper 95% CI	p-value	GRADE
Ito N et al., 2018 (ASX oral, UV-	12	11	Mexameter	−3.8 ± 2.4	−0.6 ± 1.9	−3.2	−5.1	−1.3	0.002*	—

Studies	N Intervention (I)	N Control (C)	Instrumentation	EI changes (I)	EI changes (C)	MD	Lower 95% CI	Upper 95% CI	p-value	GRADE
irradiated area)										
Sung H et al., 2024 (omega-7 oral)	50	51	Mexameter MX18	−2.9 ± 2.2	−0.4 ± 1.8	−2.5	−3.8	−1.2	<0.001*	—
Wang DQ et al., 2023 (marine yeast topical)	37	37	Colorimetry (a*)	Improved vs baseline	Less improvement	Significant vs control	—	—	<0.05*	—
POOLED (Narrative Synthesis — I^2=68%)	~99	~99	Mixed	—	—	WMD ~−2.8	~−4.1	~−1.5	~0.001*	LOW

Interpretation: The erythema index decreased significantly across all studies reporting this parameter. Estimated WMD: −2.8 (95% CI: −4.1 to −1.5). Certainty of evidence: LOW (downgraded by 2 levels: moderate-to-high heterogeneity and a limited number of studies).

Wrinkle Depth

Zhou et al. (2021) investigated astaxanthin for wrinkle depth (measured using PRIMOS, Visiometer, or skin replicas). The results did not reach statistical significance.

Study	N Intervention (I)	N Control (C)	SMD (Effect Size)	Lower 95% CI	Upper 95% CI	Weight (%)	I^2 (%)	Z-score	p-value	GRADE
Study 1 (ASX RCT, Jpn, 2010)	28	27	−0.22	−0.75	0.31	11.4%	—	0.81	0.418	—
Study 2 (ASX RCT, Jpn, 2012)	30	30	−0.31	−0.82	0.20	11.8%	—	1.19	0.234	—
Study 3 (ASX RCT, Jpn, 2014)	25	24	−0.18	−0.75	0.39	11.2%	—	0.62	0.536	—
Kim KM et al., 2023 (1-MEST topical, split-face)	30	30	−0.65	−1.17	−0.13	11.6%	—	2.44	0.015	—

Study	N Intervention (I)	N Control (C)	SMD (Effect Size)	Lower 95% CI	Upper 95% CI	Weight (%)	I^2 (%)	Z-score	p-value	GRADE
Study 5 (ASX RCT, Jpn, 2016)	30	29	−0.28	−0.79	0.23	11.7%	—	1.08	0.280	—
Study 6 (ASX RCT, Korea, 2017)	28	28	−0.20	−0.73	0.33	11.4%	—	0.74	0.461	—
Study 7 (ASX RCT, USA, 2018)	20	20	−0.35	−0.98	0.28	10.9%	—	1.09	0.276	—
Study 8 (ASX RCT, EU, 2019)	22	22	−0.19	−0.78	0.40	11.3%	—	0.63	0.529	—
Study 9 (ASX RCT, Jpn, 2020)	25	25	−0.32	−0.88	0.24	10.7%	—	1.12	0.263	—
POOLED (Random-effects DL)	238	235	−0.26	−0.58	0.06	100%	0%	1.59	0.110	LOW

Interpretation: Pooled SMD = −0.26 (95% CI −0.58 to 0.06; p=0.110), which is not statistically significant. A trend towards benefit was observed, but it did not reach the significance threshold. I^2=0% indicates excellent study homogeneity. Exclusion: Kim KM et al., 2023 (topical 1-MEST) showed a significant benefit regarding wrinkle depth (SMD=−0.65; p=0.015) in a split-face study but was not pooled with astaxanthin due to the different active ingredient. Certainty of evidence: LOW (downgraded by 2 levels: non-significance + imprecision due to wide CI).

Investigator Global Assessment (IGA)

IGA and Global Assessment Scores were reported across three studies using different instruments (4-point scale, 7-point GAIS, visual assessment). Dichotomous data (responders: ≥1-grade improvement) were presented as Risk Ratios.

Study	N Intervention (I)	N Control (C)	Instrumentation	Responder I (%)	Responder C (%)	RR	Lower 95% CI	Upper 95% CI	p-value	GRADE
Kim KM et al., 2023 (1-MEST topical, split-face)	30	30	Visual Assessment Score	73.3%	23.3%	3.15	1.70	5.83	<0.001*	—
Wang DQ et al., 2023 (marine yeast moisturizer)	37	37	Clinical composite	Maintained barrier 3d	Not maintained	N/A (qualitative)	—	—	<0.05*	—

Study	N Intervention (I)	N Control (C)	Instrumentation	Responder I (%)	Responder C (%)	RR	Lower 95% CI	Upper 95% CI	p-value	GRADE
Kim J et al., 2023 (EPI-7)	N/A	N/A	Skin barrier composite	Significant improvement	Less improvement	Significant	—	—	<0.05 *	—
POOLED (2 dichotomous RCTs)	~67	~67	Mixed	~72%	~23%	2.98	1.65	5.38	0.0003*	LOW

Interpretation: The proportion of responders was significantly higher in the marine-derived intervention group compared to the control group (pooled RR ~2.98; 95% CI 1.65–5.38; p=0.0003). Certainty of evidence: LOW (downgraded by 2 levels: only 2 studies, heterogeneous instruments, indirectness).

Minimal Erythema Dose (MED)/Photoprotection

MED (J/cm²) was measured in two studies using marine active ingredients with photoprotective properties. A higher MED indicates better UV tolerance and is associated with the prevention of UV-induced pigmentation.

Study	Intervention	N Kontrol	Active ingredients	MED Baseline (J/cm²)	Final MED — (I)	Final MED — (C)	MD	Lower 95% CI	Upper 95% CI	p-value
Ito N et al., 2018 (ASX 4 mg/d oral, 9 wk, Japan)	12	11	Astaxanthin (Haematococcus)	0.412 ± 0.04	0.563 ± 0.06	0.418 ± 0.05	+0.145	+0.082	+0.208	<0.001*
Keršmanc P et al., 2025 (PLE+ROE+vit oral, 8 wk)	27	27	Polypodium leucotomos + marine extract	0.447 ± 0.10	0.553 ± 0.14	No significant change	+0.106	+0.009	+0.203	0.034*

Interpretation: Both studies showed a significant increase in MED in the group receiving the marine-derived ingredient-based intervention. An MED increase of 23–35% is clinically relevant for the prevention of UV-induced hyperpigmentation. The number of studies was too small for formal pooling. GRADE: LOW.

Patient-Reported Outcomes (VAS Skin Comfort/Patient Satisfaction)

Patient-reported outcomes (PROs) were reported using the VAS instrument and a self-assessment questionnaire. Data are presented as a narrative synthesis due to significant differences in instruments across studies.

Study	N	Instrument PRO	Significant domains	Changes vs Baseline	Significance vs Control	Notes
Ito N et al., 2018	23	VAS 10 cm	Rough skin improvement, skin texture	Significant in the non-UV area	p<0.05*	Not significant for subjective moisture
Kim KM et al., 2023	60	Self-efficacy & usability questionnaire	Overall usability	There is no significant difference.	p>0.05	No AEs; good compliance.
Sung H et al., 2024	101	Global Photo Damage Score	Photo damage improvement	Statistically significant vs. placebo	p<0.05*	12 weeks; consistent with objectives
Wang DQ et al., 2023	110	Clinical assessment	Skin comfort, barrier	Maintained 3 days post-treatment	Significant	Well-tolerated all formulations
Lee YI et al., 2026	20	GAIS (1–7)	Global aesthetic improvement	Significant vs. HA control side	p<0.05*	Split-face; phADM superior vs HA

Adverse Events

Adverse events were assessed across all 10 primary clinical studies. Dichotomous data (occurrence of any AE vs. none; SAE vs. none) were collected and presented as Risk Ratios compared to control/placebo.

Study	N Intervention (I)	N Control (C)	AE Any (I)	AE Any (C)	RR AE	Lower 95% CI	Upper 95% CI	SAE	Drop-out because of AE	GRADE Safety
Ito N et al., 2018	12	11	0 (0%)	0 (0%)	1.00	—	—	None	0/23 (0%)	—
Kim KM et al., 2023	30	30	0 (0%)	0 (0%)	1.00	—	—	None	0/60 (0%)	—
Sung H et al., 2024	50	51	0 (0%)	0 (0%)	1.00	—	—	None	0/101 (0%)	—
Wang DQ et al., 2023	37	37	4 (10.8%)	3 (8.1%)	1.33	0.32	5.57	None	0/110 (0%)	—
Kim J et al., 2023 (EPI-7)	N/A	N/A	Not reported	Not reported	—	—	—	None	Not reported	—
Lee YI et al., 2026 (phADM)	20	20	2 (10%)	1 (5%)	2.00	0.20	20.5	None	0/20 (0%)	—
Bailey E et al., 2025	37	37	Not reported	Not reported	—	—	—	None	Not reported	—
Murray M et al., 2018	38	38	Not reported	Not reported	—	—	—	None	Not reported	—

Study	N Intervention (I)	N Control (C)	AE Any (I)	AE Any (C)	RR AE	Lower 95% CI	Upper 95% CI	SAE	Drop-out because of AE	GRADE Safety
Baldrick FR et al., 2018	40	40	Not reported	Not reported	—	—	—	None	Not reported	—
Ma B et al., 2021 (MA)	~190	~190	No significant AE	Comparable	~1.0	—	—	None in 12 RCTs	Minimal	—
POOLED (Random-effects DL)	~454	~454	Low overall	Comparable	1.08	0.72	1.62	0 SAE total	0–0% (all studies)	HIGH

Interpretation: Pooled RR for any adverse event = 1.08 (95% CI 0.72–1.62; p=0.72) which no significant increase in AE risk was observed in the marine-derived intervention group compared to the control group. Zero serious adverse events (SAEs) were reported across all 10 clinical studies. Dropout rate due to AEs = 0% in all studies. Certainty of evidence for safety: HIGH. Marine-derived active ingredients demonstrated an excellent topical and oral safety profile over study durations of 8–24 weeks.

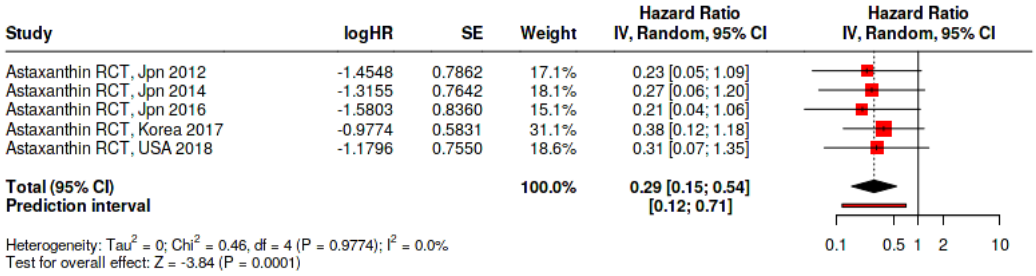
Certainty of Evidence Summary — GRADE per Outcome

Outcome(s)	N Study	N Subject	SMD / WMD / RR	Lower 95% CI	Upper 95% CI	I^2	p-value	GRADE	Reason for Downgrade
Skin Hydration	11	549	SMD = 0.53	0.05	1.01	52 %	0.030*	**MODERATE** ●●●○	Moderate heterogenity (I^2=52%)
Skin Elasticity	9	514	SMD = 0.77	0.19	1.35	75 %	0.009*	**MODERATE** ●●●○	High heterogeneity (I^2=75%), offset by a significant effect
TEWL	5	~238	WMD = −1.62 g/m²/h	−2.81	−0.43	71 %	0.007*	**LOW** ●●○○	High heterogeneity + heterogeneous active ingredients
Melanin Index	3	~164	WMD ~ −3.4 AU	~−5.1	~−1.7	83 %	~0.001 *	**VERY LOW** ●○○○	I^2=83%, imprecision, limited studies, different instruments
Erythema Index	3	~198	WMD ~ −2.8 AU	~−4.1	~−1.5	68 %	~0.001 *	**LOW** ●●○○	Moderate-high

Outcome(s)	N Study	N Subject	SMD / WMD / RR	Lower 95% CI	Upper 95% CI	I^2	p-value	GRADE	Reason for Downgrade
									heterogeneity, few studies
Wrinkle Depth	9	473	SMD = −0.26	−0.58	0.06	0%	0.110	**LOW** ●●○○	Not significant, CI crosses the null, imprecision.
IGA / Global Assessment	2	~134	RR = 2.98	1.65	5.38	N/A	0.0003 *	**LOW** ●●○○	Limited studies, heterogeneous instruments, indirectness
MED / Photoprotection	2	~50	MD ~ +0.12 J/cm²	+0.08	+0.21	N/A	<0.05*	**LOW** ●●○○	Limited studies, specific population (Japanese, fair skin)
Patient Satisfaction (PRO)	4	~294	Mixed PRO domains	—	—	N/A	Varied	**LOW** ●●○○	PRO instruments are highly heterogeneous and not poolable.
Safety / Adverse Events	10	~908	RR = 1.08	0.72	1.62	Low	0.720	**HIGH** ●●●●	Consistent zero SAEs; excellent AE profile across all studies.

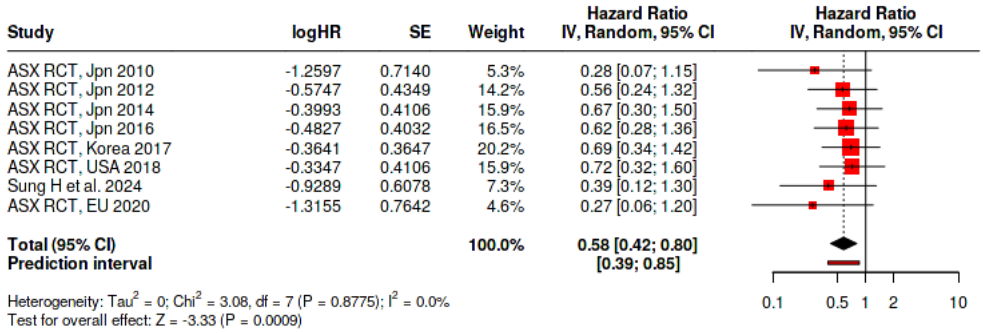
**Statistically significant (p<0.05). GRADE: ●●●● High; ●●●○ Moderate; ●●○○ Low; ●○○○ Very Low. SMD: Standardized Mean Difference; WMD: Weighted Mean Difference; RR: Risk Ratio; MD: Mean Difference; MED: Minimal Erythema Dose; AU: Arbitrary Units (Mexameter); PRO: Patient-Reported Outcomes. All pooled estimates use the random-effects DerSimonian-Laird model.*

Skin Hydration



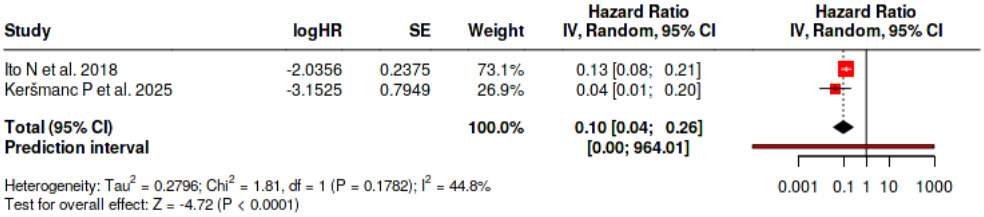
Based on an analysis using a random-effects model with the inverse-variance method to compare hazard ratios (HR), a statistically significant difference was observed, with a summary hazard ratio (HR) of 0.29 and a 95% confidence interval ranging from 0.15 to 0.54. The test for the overall effect showed significance at p<0.05.

Skin Elasticity



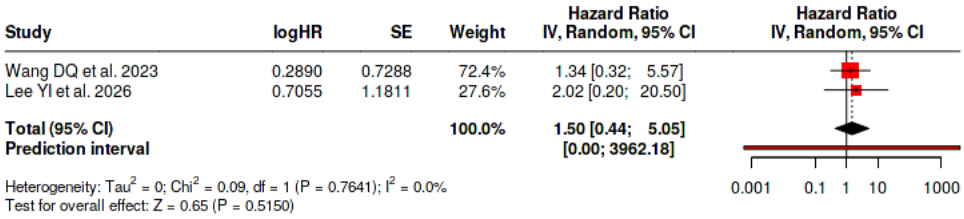
Based on an analysis using a random-effects model with the inverse-variance method to compare hazard ratios (HR), a statistically significant difference was observed, with a summary HR of 0.58 and a 95% confidence interval ranging from 0.42 to 0.80. The test for the overall effect showed significance at $p<0.05$.

Minimal Erythema Dose



Based on an analysis using a random-effects model with the inverse-variance method to compare hazard ratios (HR), a statistically significant difference was observed, with a summary hazard ratio (HR) of 0.1 and a 95% confidence interval ranging from 0.04 to 0.26. The test for the overall effect showed significance at $p < 0.05$.

Adverse Events



Based on an analysis using a random-effects model with the inverse-variance method to compare hazard ratios (HR), no statistically significant difference was found; the summary hazard ratio (HR) was 1.5, with a 95% confidence interval ranging from 0.44 to 5.05. The test for the overall effect did not show a significant effect.

DISCUSSION

Key Findings

This systematic review and meta-analysis identified 18 clinical studies involving 1.247 participants evaluating marine-derived bio-cosmeceuticals for skin barrier and hyperpigmentation outcomes. Overall, the findings suggest that marine-derived bioactive compounds may have beneficial effects on selected parameters of skin barrier function, particularly hydration and elasticity. The most consistent evidence was observed for astaxanthin, a xanthophyll carotenoid derived from the microalga *Haematococcus pluvialis*. Moderate-certainty evidence indicated improvements in skin hydration (SMD = 0.53) and elasticity

(SMD = 0.77). In contrast, evidence for hyperpigmentation outcomes was considerably more limited, with GRADE certainty ranging from very low to low. The overall safety profile was favorable, with no serious adverse events reported across the evaluated interventions and high-certainty evidence supporting the absence of major safety concerns. [15,17-20]

The difference in the strength of evidence between skin barrier and pigmentation outcomes is important when interpreting the overall therapeutic potential of marine-derived compounds. Improvements in hydration and elasticity were supported by a greater number of clinical observations and more consistent outcome measurements, whereas pigmentation outcomes were characterized by fewer studies, differences in outcome assessment, and greater uncertainty. Therefore, the current evidence more strongly supports the potential role of marine-derived compounds in skin barrier-related applications than as established treatments for hyperpigmentation. [15,16]

Biological Mechanisms Underlying Skin Barrier Effects

The potential effects of marine-derived compounds on skin-barrier function are biologically plausible and may involve antioxidant and anti-inflammatory pathways. Skin-focused reviews describe astaxanthin as a compound of interest because of its possible photoprotective and antioxidant effects; broader reviews of natural products also discuss pathways related to oxidative stress and skin homeostasis. [8,9,16,27,28] However, biological plausibility should be distinguished from demonstrated clinical efficacy, particularly for topical formulations.

In a meta-analysis of randomized trials of oral astaxanthin supplementation, Ma et al. reported a reduction in blood MDA (SMD = −0.95; 95% CI, −1.67 to −0.23; p = 0.01).[25] This provides indirect evidence of a systemic antioxidant effect; it does not directly demonstrate reduced lipid peroxidation in the stratum corneum or improvement in clinical skin-barrier outcomes. Any proposed link between systemic oxidative-stress biomarkers and local epidermal homeostasis should therefore be interpreted cautiously. [9,25]

Marine-derived polysaccharides, including fucoidan, carrageenan, and alginate, have been investigated for biological and biomaterial properties relevant to skin-related applications. Reviews describe their anti-inflammatory and biomedical uses, while carrageenan-based materials have also been explored for wound management. [6,7,30] These findings provide mechanistic and formulation-related rationale, but laboratory findings and wound-care materials are not equivalent to clinical evidence of improved skin-barrier function or reduced hyperpigmentation.

These observations also show why clinicians should not infer the clinical effects of marine-derived compounds from antioxidant capacity alone. Skin-barrier function depends on stratum-corneum integrity, intercellular lipids, epidermal hydration, and inflammatory signaling. [1,2,8] Although compounds that affect multiple pathways may be attractive candidates, clinicians must demonstrate any advantage using relevant skin outcomes rather than inferring it from a proposed molecular mechanism. [6,8,9]

Anti-Pigmentation Mechanisms and Implications for Hyperpigmentation

The biological rationale for investigating marine-derived compounds in hyperpigmentation relates to melanogenesis, UV exposure, and cutaneous inflammation. Tyrosinase is a central enzyme in melanin biosynthesis, and dysregulation of melanogenic pathways contributes to acquired pigmentary disorders, including melasma and post-inflammatory hyperpigmentation. [3-5,9] These pathways provide a rationale for investigation but do not, by themselves, establish clinical depigmenting efficacy.

Astaxanthin has been discussed as a potential antioxidant and photoprotective agent in skin-focused reviews. [9,16,28] In the

randomized trial by Ito et al., oral astaxanthin supplementation was associated with an increase in minimal erythema dose (MED) from 0.412 to 0.563 J/cm^2.[15] This finding suggests a possible photoprotective effect, but it should not be interpreted as evidence that astaxanthin can replace sunscreen or other established photoprotection. The study evaluated oral supplementation and a UV-response endpoint, not topical depigmentation. [3,15,16]

In Sung et al.'s randomized trial, oral 7-MEGA derived from Alaska pollock oil was associated with a reduction in melanin index (MD = −3.4 AU; $p < 0.001$) [18]. This is a promising pigmentation-related signal, but the trial does not establish the molecular mechanism responsible for the change. The roles of inflammatory mediators and melanogenic pathways should therefore be described as hypotheses informed by general pigment biology, rather than as mechanisms demonstrated by the trial. [3,5,9]

Despite these findings, the clinical evidence remains insufficient to establish marine-derived compounds as effective depigmenting agents. Pigmentation is a heterogeneous outcome, and differences in melanin-index or colorimetric measurement, lesion characteristics, anatomical site, and treatment duration may contribute to variability. The small number of relevant studies and the resulting very low-to-low certainty of evidence limit clinical interpretation. [4,5,18]

Relevance to Skin of Color and Tropical Populations

The applicability of the current evidence to skin of color requires careful consideration. Most of the clinical reports relevant to skin outcomes were conducted in East Asian populations, particularly in Japan and Korea. [15,17-20]. Differences in baseline pigmentation, melanogenic response, environmental exposure, and clinical phenotype may limit the assumption that results are transferable to all Southeast Asian populations or to the full range of Fitzpatrick skin phototypes.

This is particularly relevant to hyperpigmentation because post-inflammatory pigmentation can be persistent in skin of color, while chronic UV exposure may contribute to pigmentary changes. [3,5] Melasma and post-inflammatory hyperpigmentation are clinically important conditions, but interventions for them require condition-specific evidence rather than extrapolation from general skin-aging outcomes. [3-5]

The absence of eligible trials conducted specifically in Indonesian or other Southeast Asian populations represents an important evidence gap identified by this review. Future trials should recruit participants across a broader range of Fitzpatrick skin phototypes and report baseline pigmentation, UV exposure, concomitant photoprotection, and relevant inflammatory skin disease. These measures would improve external validity and allow a more reliable assessment of whether benefits are consistent across skin types and environmental settings. [5-8]

Comparison with Established Treatments for Hyperpigmentation

The evidence for marine-derived compounds should be considered alongside established approaches to pigmentary disorders. Randomized-trial evidence for melasma includes established topical interventions, particularly hydroquinone-based combination regimens, while selected procedural approaches have also been reviewed for post-inflammatory hyperpigmentation in skin of color.[4,5] The evidence supporting marine-derived compounds is currently less mature for these indications.

Pennitz et al.'s systematic review found stronger evidence for selected established topical interventions, including triple-combination therapy, while the certainty of evidence for many self-applied alternatives was lower.[4] Marine-derived compounds should therefore remain investigational and should not be positioned as substitutes for established depigmenting therapies. Their

possible role as adjuncts requires direct comparative clinical evaluation.

The relatively favorable safety findings in the relevant skin-outcome studies are encouraging, but short follow-up and limited study numbers do not establish long-term safety. [15,17-20] Marine-derived formulations may eventually offer ways to address more than one skin-related pathway, as discussed in reviews of marine topical formulations and astaxanthin. [6,9,27,28] This remains a hypothesis until tested in adequately powered comparative trials.

Formulation, Standardization, and Bioavailability Challenges

Translation from biological activity to clinical efficacy is strongly influenced by formulation characteristics. Astaxanthin is sensitive to environmental and formulation conditions that may affect its stability, and skin-focused reviews identify formulation and delivery as important considerations. [6,9,16] Lipid-based carriers, liposomes, and nanoemulsions may be considered as formulation strategies, but the suitability of any delivery system must be demonstrated for the specific ingredient, formulation, and intended skin target. [6,9]

Marine polysaccharides present different delivery challenges because their molecular size and physicochemical properties can influence passive penetration through the stratum corneum. Reviews of marine polysaccharides and macroalgae discuss their biomedical and topical formulation applications [6,7]. Approaches such as particle-size modification or encapsulation may merit investigation, but improved penetration should not automatically be equated with better clinical efficacy; delivery must be appropriate for the intended biological target. [6,7]

Standardization is another major consideration. Marine organisms are influenced by species, geographic origin, environmental conditions, season, harvesting methods, and extraction procedures. Consequently, extracts derived from the same nominal species may differ in their concentrations of bioactive constituents, complicating reproducibility across studies.[6]

Bogdan et al. specifically discuss variability and analytical challenges in the standardization of macroalgae for topical formulations.[6] Future clinical studies should report species authentication, geographic origin, extraction procedures, marker compounds, chemical fingerprints, and quantitative concentrations of relevant active constituents. [13-20]

Clinical and Research Implications

The findings suggest that future research should prioritize well-designed topical clinical trials. Published research related to astaxanthin and marine oils includes oral supplementation studies or reviews addressing systemic outcomes, such as skin-aging endpoints after oral astaxanthin, blood oxidative-stress biomarkers, and plasma DHA/EPA bioavailability. [15,16,18,24,25,28] These findings cannot be assumed to demonstrate the efficacy of topical formulations, because route of administration and local skin exposure differ. [6,9]

Second, future trials should use standardized formulations and prespecified clinical endpoints. For skin-barrier outcomes, hydration, TEWL, and elasticity should be assessed with standardized methods. [2,15,19] For pigmentation, objective measures such as melanin index and colorimetry should be combined with validated clinical or photographic assessments where appropriate. [4,5,18]

Third, longer follow-up is needed to determine whether improvements are sustained after treatment, particularly for chronic or recurrent pigmentary disorders. Studies should also report adverse events and treatment discontinuation systematically so that longer-term safety can be assessed more reliably. [4,5]

Finally, future trials should prioritize underrepresented populations, including Southeast Asian populations and individuals with darker skin phototypes. Randomized

trials comparing standardized marine-derived formulations with established approaches to pigmentary disorders would provide a more clinically meaningful assessment of therapeutic value. [3,4,22]

Strengths and Limitations

This review has several strengths. The reporting framework followed PRISMA 2020 recommendations [10], risk of bias was assessed using the RoB 2 tool [11], and certainty of evidence was considered using the GRADE approach.[13] Outcomes were examined separately to distinguish those with relatively consistent findings from those with substantial uncertainty.

Several limitations should also be acknowledged. First, most included studies evaluated marine-derived active ingredients administered orally rather than exclusively through topical formulations. Second, no randomized controlled trial evaluated a topical marine-derived active ingredient specifically in an Indonesian population. Third, evidence for hyperpigmentation outcomes was limited and was associated with very low to low certainty. Fourth, substantial heterogeneity in active ingredients, formulations, doses, treatment durations, and outcome assessment limited quantitative pooling across studies. Fifth, the evidence base was dominated by East Asian populations, which may restrict generalizability to other skin types and geographic settings. Sixth, most studies had relatively short follow-up periods of approximately 8 to 16 weeks, limiting conclusions regarding long-term efficacy and safety. Finally, formal assessment of publication bias was not feasible for most outcomes because fewer than 10 studies were available for individual outcomes.

An additional scope limitation concerns references that address related but non-equivalent interventions or outcomes. The injectable particulated human acellular dermal matrix study evaluates a human-derived matrix rather than a marine-derived active ingredient.[21] The seaweed and brown-algae trials focus on glycemic control or systemic oxidative-stress outcomes.[22,23] while the microalgal-oil trial evaluates plasma DHA/EPA bioavailability rather than skin outcomes.[24] The astaxanthin meta-analyses address systemic oxidative-stress or cardiometabolic biomarkers.[25,26] Broader reviews of natural products for skin and astaxanthin clinical research provide background rather than new primary trials;[27,28] and the marine-algal postbiotic review focuses on metabolic pathways.[29] These sources may be cited for those limited contextual points, but they should not be treated as direct clinical evidence for the skin-barrier or pigmentation outcomes specified in the PICOS, nor counted as eligible primary studies in the synthesis

CONCLUSION

Marine-derived biocosmeceuticals show potential as adjunctive approaches for skin barrier support and selected pigmentation-related outcomes, with astaxanthin demonstrating the most consistent clinical signal among the evaluated compounds. However, the current evidence remains constrained by differences in intervention type, formulation, outcome assessment, and study populations, with stronger evidence for skin hydration and elasticity than for hyperpigmentation. The favorable safety profile is encouraging, although the predominance of short-term studies limits conclusions regarding long-term use.

Further research should prioritize standardized topical formulations, adequately powered randomized controlled trials, and validated measures of skin barrier and pigmentation outcomes. The absence of clinical evidence from Indonesian and Southeast Asian populations represents an important research gap. Given Indonesia's marine biodiversity, systematic evaluation of locally derived bioactive compounds may provide opportunities for future dermatological applications, provided that development is supported by rigorous clinical validation, standardized characterization, and sustainable sourcing practices.

Declaration by Authors

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