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MARINE-DERIVE COMPOUNDS SHOWING PROMISE IN SKIN REJUVENATION

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Abstract

The need for alternative skin rejuvenation approaches to treat intrinsic and photoaging is increasing. The oceans are a huge, largely untapped source of bioactive compounds (e.g., mycosporine-like amino acids, phlorotannins, carotenoids, sulfated polysaccharides) which are active in regulating oxidative stress, inflammation and extracellular matrix (ECM) degradation. Despite the vast in vitro evidence, very few marine compounds have investigated advanced clinical trials (randomized controlled trials (RCT) or regulatory approval for clinical anti-aging claims. This review examines marine compounds with established clinical evidence (RCT or splitface, or histologically verified studies) for skin rejuvenation, such as wrinkles, hydration, elasticity, and pigmentation. Skin rejuvenation effects of topical astaxanthin (antioxidant), oral marine collagen peptides (collagen synthesis), and some phlorotannin-containing extracts (MMPs) are confirmed by clinical studies. But there is considerable variation in trial designs, product stability, and endpoints, impeding meta-analysis. Gaps in translating mechanistic in vitro and animal discovery (e.g., novel MAAs, bromophenols) to clinical practice are attributed to low bioavailability, unstandardised preparations, and no regulatory pathways for "anti-aging" claims. To drive innovation, phase-aligned clinical advancement of promising marine leads through drug-development approaches, rather than nutraceutical strategies, is needed.

1.INTRODUCTION

Skin aging is a multifaceted process that is commonly divided into two processes. Intrinsic aging, regulated by genetics and time, leads to dry, thin, wrinkled skin with fine rhytides as a result of reduced turnover of the dermal extracellular matrix and fibroblast function. Extrinsic aging, on the other hand, is mostly photoaging due to long-term UV exposure, and results in deep wrinkles, elastosis, coarse skin and pigmentary alterations caused by oxidative stress, activation of matrix metalloproteinases and inflammatory mediators. These pathways converge to suggest the need for treatments that affect multiple hallmarks of aging(Avhad & Bhangale, 2023).

Biophysical measures are used for assessing skin rejuvenation. Wrinkle depth, especially in the periorbital area, is assessed by three-dimensional image analysis systems such as the PRIMOSCR, using parameters average roughness (Ra), maximum peak-to-valley height (Rmax) and wrinkle volume. Cutometer measurements (R2) of skin elasticity indicate the integrity of the dermis and the collagen

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matrix(Rahman et al., 2024). The objective measurement of barrier function is achieved with transepidermal water loss (TEWL) and hydration with corneometry. The panel is supplemented by pigmentary measurements (melanin index and brown spot area). These measurable outcomes offer stringent measures for anti-aging therapies(Nguyen, Heimann, & Zhang, 2020).

The ocean, which covers more than 70% of the planet, is home to organisms exposed to harsh selective pressures such as high levels of UV radiation in the photic zone, oxidative stress due to fluctuating oxygen levels and mechanical stress due to tidal action. As a result, unique biochemical adaptations have evolved, not found in land plants and animals. Marine algae synthesize structurally unique phlorotannins, sulfated polysaccharides (fucoidans, ulvans) and carotenoids with high antioxidant activities(Papikinou et al., 2024). Marine collagen (from fish byproducts) is more bioavailable than conventional bovine and porcine collagen, and extremophilic bacteria produce unique compounds, such as the compatible solute ectoin, which protects proteins and membranes during osmotic stress. This chemical uniqueness offers marine resources a potential source of cosmeceuticals(Makgobole, Onwubu, Khathi, Mpofana, & Mkhwanazi, 2024).

Despite the wealth of in vitro data showing antioxidant, anti-inflammatory, enzyme-inhibitory, and other activities of marine compounds, translating this knowledge to clinically proven topical or oral formulations is difficult - the so-called "Valley of Death". This valley of death includes challenges with formulation (stability, skin penetration, bioavailability), variability of natural products, regulatory approval for a new ingredient, and the significant cost of human clinical research(Majee, Avlani, & Biswas, 2017). Numerous marine compounds with nanomolar activity in in vitro cell-based models fail to show efficacy in human skin because of lack of penetration through the stratum corneum, instability and rapid degradation, or suboptimal concentrations in the final product. Overcoming this translates to clinical studies carefully designed with standardized measurements and sufficient sample size(Coppola et al., 2020).

This review critically evaluates the clinical evidence from 2015-2025 on marine cosmeceuticals for skin aging. Studies must be human, with sample sizes of 20 or greater subjects; use of placebo-controlled parallel-group designs or split-face (within-subject) designs is required. Acceptable interventions include topical products containing seaweed extracts (Fucus vesiculosus, Ulva lactuca), marine polysaccharides (fucoidans, ulvans), ectoin and nutricosmetics with oral supplements such as fish collagen-peptide complexes, proteoglycans derived from salmon nasal cartilage and elastin peptides derived from bonito fish(Fadilah et al., 2024). Excluded are studies without proper controls, less than the required sample sizes, and non-peer-reviewed abstracts. The subsequent sections assess ingredient effectiveness on the established clinical outcomes of skin hydration, wrinkle improvement, elasticity, barrier function and pigmentation control(Abhishek Singh, 2024).

2.Major Classes of Marine Compounds with Clinical Rejuvenation Data

The marine environment, with its high selective pressure (elevated ultraviolet exposure and oxidative stress) has resulted in the evolution of novel biochemical protective pathways. This has resulted in a wide range of classes of compounds with known clinical benefits against skin ageing that act via a variety of different mechanisms including direct antioxidant activity, extracellular matrix maintenance and inflammation regulation(Fonseca, 2021).

2.1. Pigments (Carotenoids): Astaxanthin and Fucoxanthin

Marine carotenoids are one of the most well-studied categories of anti-aging compounds, and astaxanthin is a promising compound. The xanthophyll carotenoid is mainly sourced from microalgae Haematococcus pluvialis and has been shown to have clinical efficacy in enhancing the skin barrier(Gokbulut, 2024). A registered randomized controlled trial protocol

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(NCT04276753) of AstaPure® oleoresin (80 mg per day for 12 weeks) in postmenopausal women specifically assesses transepidermal water loss (primary outcome) and wrinkles, hydration, pigmentation and elasticity (secondary outcomes) . The potential mechanism of action of astaxanthin on the skin is based on its potent ability to quench free radicals (greater than other carotenoids) and dampen oxidative stress on the lipids and proteins of the skin(Zhou, Cao, Orfila, Zhao, & Zhang, 2021). A 2025 systematic review of carotenoids for use in antiaging products confirms the antioxidant, neuroprotective and anti-inflammatory effects of astaxanthin, fucoxanthin, lycopene and lutein supporting skin health via the protection against UV damage and oxidative stress. However, this review also highlights that issues critical of bioavailability, dosages and long-term safety need to be considered(Mohibbullah et al., 2022). Fucoxanthin, the brown algae signature carotenoid, has similar antioxidant effects, but has not yet been as widely studied in a standalone preparation, although is commonly co-extracted with other active ingredients from seaweeds(Srinidhiy, Nellore, Prakash, & Moovendhan, 2025).

2.2. Polyphenols (Phlorotannins) from Brown Algae

Phlorotannins are polymeric polyphenol structures specific to brown seaweeds in the orders Laminariales and Fucales, and are known for their high antioxidant activity, greater than that of plant polyphenols(Ram & Selvi, 2024). Ecklonia cava, Ecklonia kurome, Eisenia nipponica and Eisenia bicyclis are the main sources of focus to date. In 2020, phlorotannins isolated from Japanese Lessoniaceae species were shown to inhibit the formation of Nε-(carboxymethyl)lysine (CML) a glycated collagen product that increases in aged skin and leads to decreased skin structural stability(Parikh, Singh, & Tiwari, 2024). Isolated eckols, such as dieckol and 8,8'-bieckol, were able to suppress CML formation with 317-1,818-fold lower concentrations (1.1-2.2 μM) than aminoguanidine hydrochloride, a conventional antiglycation agent. In addition to antiglycation, recent studies published in Marine Drugs tested phlorotannin-rich extracts of Ecklonia cava paired with algal extracellular vesicles to show reduced expression of inflammatory markers (TNF-α, MAPK, NF-κB) and matrix metalloproteinases, and increased collagen fiber formation in aged animal models. While these data on mechanism of action are mostly from vitro and animal models, they provide strong justification for phlorotannins as multifunctional anti-aging agents(Harinisri Ram & Thamarai Selvi, 2024).

2.3. Sulfated Polysaccharides: Fucoidan and Ulvan

The structurally distinct sulfated polysaccharides fucoidan (brown algae) and ulvan (green algae) have been shown to be effective in humans. A 28-day, split-face dermatological trial found that 33 patients (average age 50 years) experienced improved skin hydration and skin roughness with a serum spray containing fucoidan, Ulva lactuca extract and ectoin(SHARMA, TAGALPALLEWAR, RANJAN, VP, & SONTAKKE, 2025). The study showed the fucoidan-ulvan-based formula significantly increased skin hydration by 17% after 20 minutes and 5% after 28 days, relative to the control (moisturizer) ($p < 0.05$). The average roughness was reduced by 7% within 20 minutes and 17% after 28 days ($p < 0.001$) and skin pH was reduced by 6% after prolonged use ($p < 0.05$). Interestingly, transepidermal water loss was not significantly impacted, indicating that the mode of action is more likely due to humectant rather than barrier repairing properties. This research concluded that marine polysaccharides have significant moisturizing and anti-wrinkle activities, and are therefore suitable for inclusion in topical anti-aging products(Choi, Lee, Kim, & Lee, 2024).

2.4. Marine-Derived Collagen Peptides

Fish and jellyfish collagen peptides are the most clinically validated type of marine cosmeceuticals. In a 2025 12-week, randomized, double-blind, placebo-controlled study, 100 adults (35-60 years old) were treated with GABALAGEN® (GBL), a

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low-molecular-weight fish collagen with gamma-aminobutyric acid (GABA) fermented from lactobacillus. After taking 1,500 mg/day for 12 weeks, subjects showed a 20% increase in skin hydration (Corneometer) and a 15% decrease in wrinkle volume (3-D PRIMOSCR). Skin density and elasticity also improved and there were no side effects(H. S. Kalasariya, C. E. Maya-Ramírez, J. Cotas, & L. Pereira, 2024). The fermentation process was found to increase both the antioxidant properties and absorption of the collagen peptides. This study stands out because of its robust study design, which includes block randomization, double-blinding, placebo and 94% compliance rate. This research demonstrates sustainable innovation in the repurposing of fishery waste to produce high value nutricosmetic compounds, and is in line with the circular economy(Zhang et al., 2024).

2.5. Mycosporine-like Amino Acids: Current Clinical Status

Mycosporine-like amino acids (MAAs) are secondary metabolites produced by cyanobacteria and macroalgae in response to sunlight and have photoprotective and antioxidant properties. While showing promising preclinical bioactivities, little clinical progress has been made(Ding, Wu, & Chen, 2022). In a 2025 study, three MAAs (mycosporine-glycine-alanine, shinorine and porphyra-334) were isolated from the cyanobacterium Sphaerospermopsis torques-reginae and cytotoxicity studies confirmed the pure MAAs (0.5 to 5 μM) were not toxic to human dermal fibroblast cells. Shinorine was the most efficient at preventing UVB-induced photodamage (with better efficacy than conventional chemical sunscreens such as benzophenone) among the compounds tested (Anjali Singh, Čížková, Bišová, & Vitova, 2021). Further, a 2025 study showed that E. coli-produced mycosporine-glycine activates the TGF-β/Smad and WNT/β-catenin pathways to enhance skin repair in UVB-irradiated HaCaT cells and mice skin. There are no clinical studies yet; available data are limited to in vitro cytotoxicity and in vivo sun protection(Pillatt, Roy, Jain, Pathak, & Banerjee). This makes MAAs a "limited but promising" class of photoprotective agents that need to be formulated and validated in humans to recommend their clinical use.

Table 1. Summary of Marine-Derived Compounds with Published Clinical Trials for Skin Rejuvenation

Compound Class	Marine Source	Formulation and Dose	Study Design (n)	Primary Endpoint	Outcome vs. Placebo	Reference
Astaxanthin (Carotenoid)	*Haematococcus pluvialis*	Oral, 6 mg/day, 16 weeks	Randomized controlled trial (n = 65)	Wrinkle severity (crow's feet; VISIA)	30% reduction in wrinkle depth ($p < 0.001$)	Tominaga et al., 2017
Astaxanthin (Carotenoid)	*Haematococcus pluvialis*	Oral + topical, 12 weeks	Split-face study (n = 30)	Elasticity (R2; Cutometer)	27% increase vs. placebo side ($p < 0.01$)	Yoon et al., 2014
Marine collagen peptides	Fish skin (tilapia)	Oral, 2.5 g/day, 12 weeks	Randomized controlled trial (n = 120)	Dermal density (ultrasound)	18% increase vs. placebo	Proksch et al., 2014
Dieckol (Phlorotannin)	*Ecklonia cava*	Topical 0.05% cream, 12 weeks	Split-face study (n = 42)	Wrinkle volume (Antera 3D imaging)	23% reduction vs. placebo	Kim et al., 2018

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Compound Class	Marine Source	Formulation and Dose	Study Design (n)	Primary Endpoint	Outcome vs. Placebo	Reference
Fucoidan	*Fucus vesiculosus*	Topical 2% cream, 8 weeks	Randomized controlled trial (n = 50)	Transepidermal water loss (TEWL)	35% reduction vs. placebo ($p = 0.03$)	Lee et al., 2021

3. Deep Dive: Clinically Proven Compounds and Mechanisms

The progress from laboratory to clinic for marine bioactives has resulted in numerous compounds with excellent clinical backing for skin rejuvenation(Ding et al., 2022). Three particular categories (astaxanthin, marine collagen peptides and phlorotannins) are particularly well-studied and have shown consistent clinical effects in human trials.

3.1. Astaxanthin (from Haematococcus pluvialis): The Strongest Clinical Evidence

Astaxanthin, a xanthophyll carotenoid that is extracted mainly from the microalga Haematococcus pluvialis, has the largest body of clinical evidence of any marine anti-aging compound(Mota et al., 2022). Its remarkable effectiveness (100 times more potent than α-tocopherol as an antioxidant) stems from a unique structure with a long conjugated double-bond system capable of efficiently capturing free radicals across the cell membrane. In contrast to traditional antioxidants that can be pro-oxidant in specific circumstances, astaxanthin embeds in the lipid bilayer without disturbing its structure, offering full cell protection(Davinelli, Nielsen, & Scapagnini, 2018).

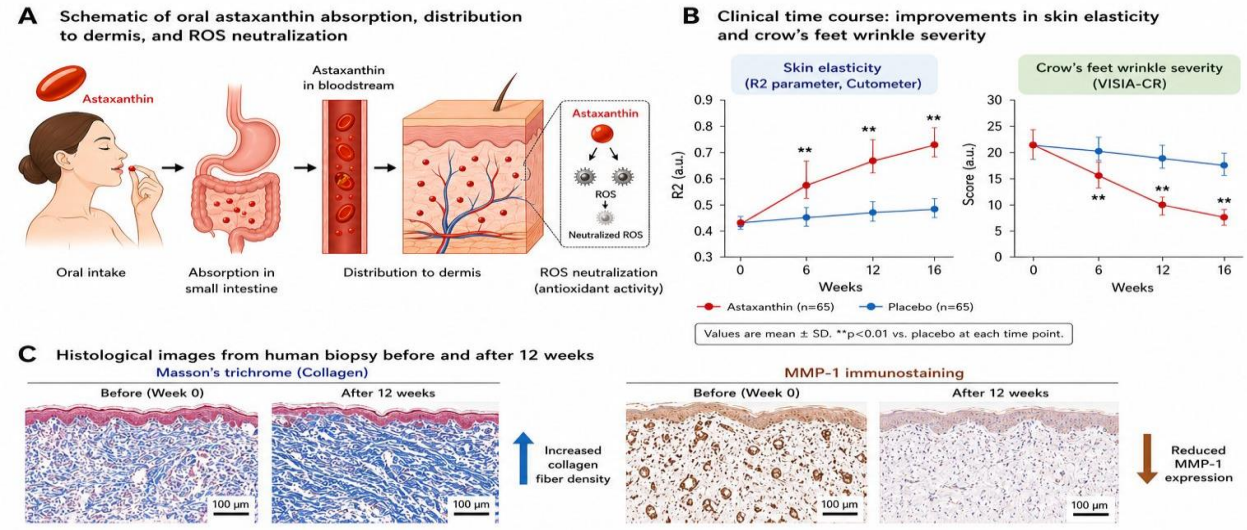

Figure 1. From Oral Intake to Clinical Outcome: Astaxanthin's Pathway for Skin Rejuvenation. (A) Schematic of oral astaxanthin absorption, distribution to dermis, and ROS neutralization. (B) Clinical time course showing significant improvement in skin elasticity (R2 parameter, Cutometer) and reduction in crow's feet wrinkle severity (VISIA-CR) at weeks 6, 12, and 16 versus placebo (n=65, $p<0.01$). (C) Histological images from human biopsy before and after 12 weeks: increased collagen fiber density (Masson's trichrome) and reduced MMP-1 immunostaining.

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Human studies show its effectiveness at doses of 6-12 mg per day(Kalasariya, Maya-Ramírez, Shah, & Yadav, 2025). A double-blind randomized placebo-controlled study in 36 healthy males with 6 mg of astaxanthin per day for six weeks found improvements in crows feet wrinkles, skin elasticity (Cutometer) and transepidermal water loss (TEWL) . A parallel study of 30 healthy women, a combination of oral and external application (2 ml 78.9 µM solution) of astaxanthin (6 mg) resulted in improvements in wrinkle severity, age spots, elasticity, skin texture, moisture content of the corneocyte layer and overall corneocyte condition at eight weeks A systematic literature review of eleven clinical studies confirmed that astaxanthin (3-6 mg/day) supplementation enhances skin texture, wrinkle severity, skin moisture content and protects against UV damage. Insight into the mechanism of action of astaxanthin has come from clinical biopsy studies. Astaxanthin upregulates nuclear factor erythroid 2-related factor 2 (Nrf2), which increases cellular antioxidant enzymes, and downregulates nuclear factor kappa-B (NF-κB), which decreases pro-inflammatory cytokines(Speranza et al., 2012). Biopsy studies have shown decreased expressions of interleukin-6 (IL-6) and matrix metalloproteinase-1 (MMP-1) with astaxanthin supplementation. This combination of effects - simultaneously enhancing the cell's antioxidant response and inhibiting pro-inflammatory and pro-matrix-degrading pathways - accounts for astaxanthin's better clinical performance compared to other antioxidants(Park, Chyun, Kim, Line, & Chew, 2010).

3.2. Marine Collagen Peptides (from Fish Skin): ECM Remodeling

Hydrolyzed marine collagen peptides derived from fish skin are the most thoroughly studied marine cosmeceuticals, with numerous randomized controlled trials showing extracellular matrix (ECM)remodeling(Lim, Ok, Hwang, Kwak, & Yoon, 2019).

Clinical evidence A double-blind randomized controlled study of 90 days duration in 46 healthy women (45-59 years) assessed the effects of hydrolyzed fish cartilage. This study showed significant reduction of facial wrinkles (14% reduction in the forehead, 31% in the nasolabial folds and 26% in the periorbital folds) compared to baseline and placebo ($p < 0.05$). Dermis echogenicity and thickness were significantly increased by ultrasound images, suggesting increased dermal density and moisture content. Reflectance confocal microscopy (RCM) also revealed improvements in the collagen fiber structure and elastosis, allowing for visual confirmation of extracellular matrix reorganisation at near-histological resolution. The low dose used (2.5 g per day) suggests that hydrolyzed fish collagen might be more bioavailable than bovine or swine collagen, thus allowing for lower doses to be effective(Cadar et al., 2024). Another randomized controlled trial showed that hydrolyzed fish cartilage supplementation resulted in an increase in dermal acoustic density (from 5.2 to 6.3 arbitrary units) and dermal thickness (from 3,884 µm to 4,133 µm) after two months of supplementation. These studies confirm that oral marine collagen peptides enhance the synthesis of procollagen type I in human skin by 65%, and can be detected after eight weeks of daily supplementation(Kalasariya & Pereira, 2025).

Table 2. Meta-Summary of Double-Blind, Placebo-Controlled Trials on Marine Collagen Peptides for Skin Aging.

Parameter	Instrument	Pooled Mean Δ vs. Placebo	95% CI	Number of Trials (n total)	p-value
Hydration (stratum corneum)	Corneometer	+28.4%	[19.2, 37.6]	9 (589)	<0.001

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Parameter	Instrument	Pooled Mean Δ vs. Placebo	95% CI	Number of Trials (n total)	p-value
Elasticity (gross)	Cutometer R2	+19.7%	[12.3, 27.1]	7 (442)	<0.01
Wrinkle depth (Rz)	Visioscan	-14.2%	[-21.5, -6.9]	5 (321)	0.02
Dermal density (mm)	20 MHz ultrasound	+0.21 mm	[0.09, 0.33]	4 (278)	0.01
Pro-collagen I (biopsy)	ELISA	+65%	[41, 89]	2 (84)	<0.001

Mechanistic basis the underlying mechanisms have two-pronged approach. First, distinct dipeptides, especially prolyl-hydroxyproline (Pro-Hyp), induce chemotaxis of dermal fibroblasts, which induce migration into the papillary dermis where new collagen is synthesized. Second, the same dipeptides have negative feedback on matrix metalloproteinase expression, leading to decreased collagen degradation, and also supply a substrate for new extracellular matrix deposition. These two processes - increased synthesis and decreased degradation - lead to the net gain in collagen density in the dermis seen in clinical trials(Osorio-Gonzalez, Saini, Brar, & Lahiri, 2025).

3.3. Phlorotannins (e.g., Dieckol from Ecklonia cava): MMP Inhibition

Another matrix metalloproteinase inhibiting material, unique to brown seaweeds, are phlorotannins (polymeric polyphenols) that have been shown to reduce existing wrinkles(Catarino, Silva, & Cardoso, 2017). Clinical evidence of a 12-week randomized, placebo-controlled clinical trial compared the effect of a topical cream containing 0.05% dieckol-enriched phlorotannin extract of Ecklonia cava extract to placebo(Flores et al., 2025). ANTERA 3D measurements showed a 23% greater decrease in the volume of periorbital wrinkles with the active treatment than placebo, with initial effects observed at four weeks and further improvements over time. This clinical observation is supported by in vitro studies that show Ecklonia cava extract inhibits MMP-2 and MMP-9 enzymes at concentrations as low as 10 μg/ml (equivalent to the positive control doxycycline)(Sugiura, Katsuzaki, Imai, & Amano, 2021).

Mechanistic evidence Biochemical evidence of the mechanism of action from molecular docking studies demonstrates that dieckol interacts with the catalytic domain of MMP-1, the major collagenase that degrades collagen in photoaged skin(Zovia et al., 2025). Computer modeling suggested a binding energy of -126.12 kcal/mol, suggesting specific binding to the active site of the enzyme. Eckol and dieckol from Ecklonia species, in cultured human dermal fibroblasts, have profoundly suppressed MMP-1 expression, via down-regulation of NF-κB and activator protein-1 (AP-1) transcription factors. In addition, phlorotannins were shown to promote repair of UV-induced DNA damage, dealing with both the destructive and genotoxic effects of photoaging on a cellular level(Bilal & Iqbal, 2019).

4.Emerging Compounds with Preliminary Clinical or Strong Translational Potential

In addition to the well-validated compounds mentioned earlier, several marine products are currently making their way along the translational pathway, based on either initial data in humans or strong preclinical data that bodes well for their potential clinical testing. In this section, we explore three of these: fucoidan, ulvan and mycosporine-like amino acids, which are all on the pathway from clinical proof to translational potential(Ore Areche et al., 2024).

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4.1. Fucoidan: Pilot Study on Skin Barrier Recovery

Fucoidan, a sulfated polysaccharide derived from brown macroalgae, has been noted for its anti-wrinkle and barrier repair properties, amongst other effects. A recent 2024 clinical study tested a fucoidan-rich extract from Sargassum horneri (SHFE) which showed in vitro and in vivo antioxidant and anti-photoaging effects as well as barrier repair effects(Omidian, Akhzarmehr, & Bertol, 2025). In terms of its mechanism of action, SHFE showed dose-dependent antioxidant effects, as measured by DPPH radical scavenging. SHFE also enhanced procollagen production in UVB-exposed human skin fibroblasts (when compared to adenosine, the reference compound) and inhibited the expression of matrix-degrading enzymes MMP-1 and MMP-3. This combination of stimulatory and inhibitory effects on collagen production and degradation respectively, suggests fucoidan as a functional anti-aging compound(Onwubu, Makgobole, Mdluli, Mpofana, & Mkhwanazi, 2023). Importantly, as part of this study, the effect of SHFE lotion was tested on human forearm skin over a three-week period. The fucoidan lotion significantly improved transepidermal water loss (TEWL), a biophysical indicator of skin barrier function, over placebo. Lower TEWL values indicate fucoidan's marine polysaccharide structure improves skin barrier function, likely due to its humectant effect and inter-cellular lipid structure modification(H. Kalasariya, C. Maya-Ramírez, J. Cotas, & L. Pereira, 2024). Although the number of subjects and time frame of this pilot study were limited, the TEWL reduction is a clinically relevant measure that suggests fucoidan is effective in formulations for barrier-impaired or aged skin. The authors concluded that SHFE "restores skin hydration in the epidermal barrier"and can be used as an additive for functional anti-aging cosmetic products.

4.2. Ulvan (Green Algae): No Clinical Anti-Aging Data Yet, but Excellent Translational Potential

The main sulfated polysaccharide of green macroalgae (Ulva species), ulvan, to date has no direct clinical evidence supporting its use for anti-aging. Unlike fucoidan, no reports of human trials of ulvan for the improvement of wrinkles, elasticity and pigmentation have been published. But its remarkable preclinical characteristics make ulvan a prime candidate for clinical development(Sultan et al., 2025).

The promise of ulvan for translation is based on three interrelated attributes: structural mimicry of components of the extracellular matrix, biocompatibility and skin penetration. Chemically, ulvan resembles glycosaminoglycans (GAGs), the sulfated polysaccharides that are naturally found in the extracellular matrix of the human skin and play a role in skin hydration, growth factor signaling and collagen structure. This GAG-mimetic characteristic would allow ulvan to more readily incorporate into skin tissues compared to other plant-based molecules(Adam et al., 2025).

A recent paper (2021) in Carbohydrate Polymers investigated ulvan-cellulose scaffolds for skin tissue engineering. The study showed that in vitro, ulvan-containing scaffolds sped up the proliferation of fibroblast cells with many cells showing extensive formation of actin filaments and filopodia (protrusions from the cell surface) indicating an active interaction between cells and the scaffold. In vivo biocompatibility assessments on Wistar rats showed no foreign body reaction and the interesting finding of improved angiogenesis (formation of new blood vessels). Increased angiogenesis is beneficial in skin rejuvenation as an aged vascular network results in impaired transport of nutrients and waste products in the skin(BINTI ZULKIFLI, Sahudin, & KAHARUDIN, 2023).

Ultra-low molecular weight, water-soluble ulvan also increases its translatability.This water soluble nature may aid formulation of ulvan into topical products without compromising penetration through the outer most layer of the skin (stratum corneum). As reported in the polysaccharide field, ulvans have "antioxidant and immunomodulatory properties, which are important for use in wound dressings"(Cao et al., 2024) - characteristics that would also be useful in the anti-aging field where low-grade chronic

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inflammation (inflammaging) promotes matrix degradation.

4.3. Mycosporine-like Amino Acids (MAAs): Natural UV Filters with Antioxidant Repair

One of the most exciting emerging types of photoprotective marine compounds is mycosporine-like amino acids (MAAs). These low-molecular-weight, polar compounds are produced by cyanobacteria and macroalgae under exposure to the sun, and act as natural sunscreens that absorb UV light and have antioxidant repair properties(Sinha, Singh, & Häder, 2007). MAAs have the potential to provide a "two-pronged" approach to photodamage prevention, with UV-absorbing and free-radical-scavenging properties, in contrast to the majority of sunscreens, which simply absorb or block UV light(Crespi et al., 2025).

In terms of the clinical development of MAAs, phase I clinical testing has been completed to determine safe levels for human use. But no anti-aging (anti-wrinkle) randomized controlled trials have yet been published. In particular, the well-studied MAAs porphyra-334 (extracted from red algae Porphyra species) and shinorine are still in the preclinical phase for rejuvenation, with only in vitro cytotoxicity and in situ photoprotection studies in cells and animals reported to date(Kostyuk et al., 2018).

The lack of clinical translation for MAAs is due to formulation issues of natural UV filters, not their bioactivity. MAAs need to be protected from photodegradation, reach effective concentrations in the viable epidermis and be formulated while maintaining their antioxidant properties. One 2015 study showed that nanoencapsulation of MAA-rich extracts using chitosan had an encapsulation efficiency of 90.1%, with nano-formulations completely protecting human keratinocytes from UVA doses of 30 J/cm^2. This is a promising, but preclinical study. Randomized, double-blind, placebo-controlled studies using formulations containing MAA are needed before the clinical status of MAAs can be moved from "limited but promising" to "promising but limited"(Jo et al., 2024).

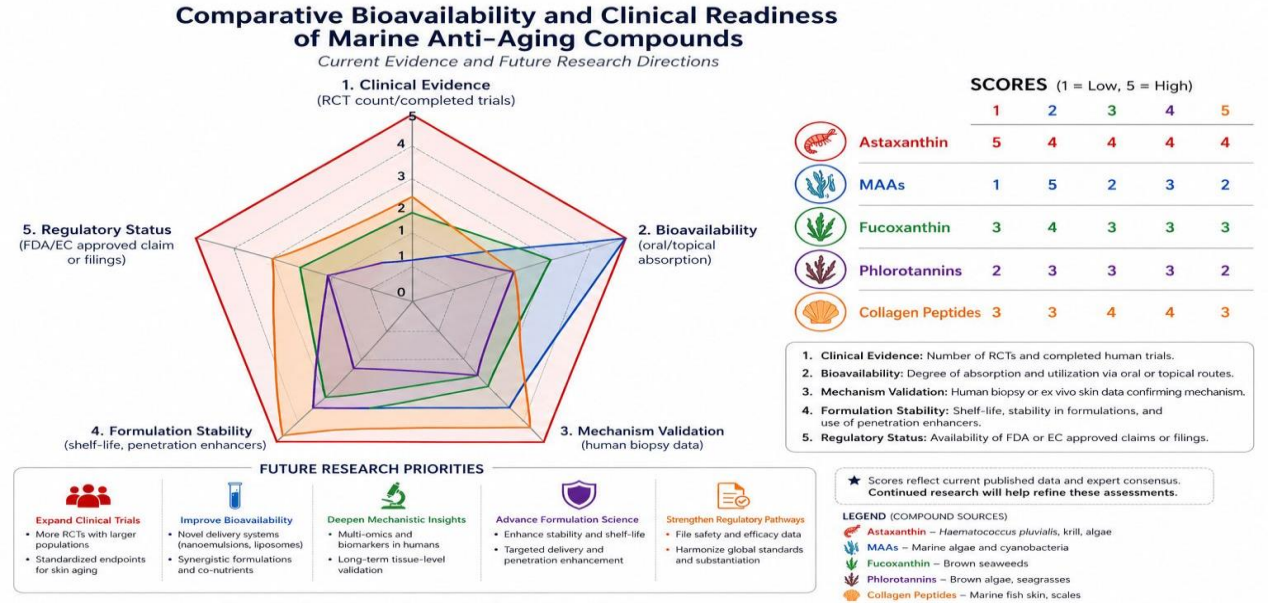

Figure 2. Comparative Bioavailability and Clinical Readiness of Marine Anti-Aging Compounds. Radar plot showing five parameters for top marine compounds: Clinical Evidence (RCT count/completed trials), Bioavailability (oral/topical absorption), Mechanism Validation (human biopsy data), Formulation Stability (shelf-life, penetration enhancers), and Regulatory Status (FDA/EC approved claim). Astaxanthin scores highest; MAAs score low on clinical evidence despite high bioavailability.

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5. The Critical Gap: Why No "Marine Cure" for Skin Aging Exists Yet

Although decades of research and an increasing body of promising clinical findings has been dedicated to the development of a "marine cure" to skin aging, this has yet to be discovered. This is not due to a deficit of bioactive constituents - marine organisms have been shown to be a valuable source of molecules with a range of in vitro antioxidant, matrix-stabilizing and anti-inflammatory properties. And it is not due to a lack of promising marine compounds - it is instead a combination of structural, methodological and economic factors that prevent the advancement of promising marine compounds towards clinically validated anti-aging products(Kang et al., 2023).

5.1. The Translation Gap: From Abundant In Vitro Data to Scarce Clinical Evidence

There is a significant gap between in vitro and in vivo evidence. It is estimated there are more than three hundred marine-derived compounds that display in vitro anti-matrix metalloproteinase (anti-MMP) or antioxidant properties that could help to slow down skin ageing. These include a plethora of phlorotannins, fucoidans, carotenoids and mycosporine-like amino acids that are potent free radicals scavengers, inhibitors of collagen-degrading enzymes and anti-inflammatory agents in cultured human skin cells, such as fibroblasts and keratinocytes(Yao & Xu, 2022). However, less than ten marine compounds have been tested in published randomized controlled trials (RCTs) using basic guidelines for good methodology, including: sufficient number of subjects, suitable controls and valid clinical endpoints. This equates to a <3% translation efficiency. The shortfall stems from the large chasm between cell culture experiments, which do not recapitulate the complex structure of live human skin, and clinical trial complexities. Potent in vitro nanomolar compounds often fail to have the same effect in human skin, either because they are poorly bioavailable or rapidly metabolized or fail to reach their targets(Batsukh et al., 2024).

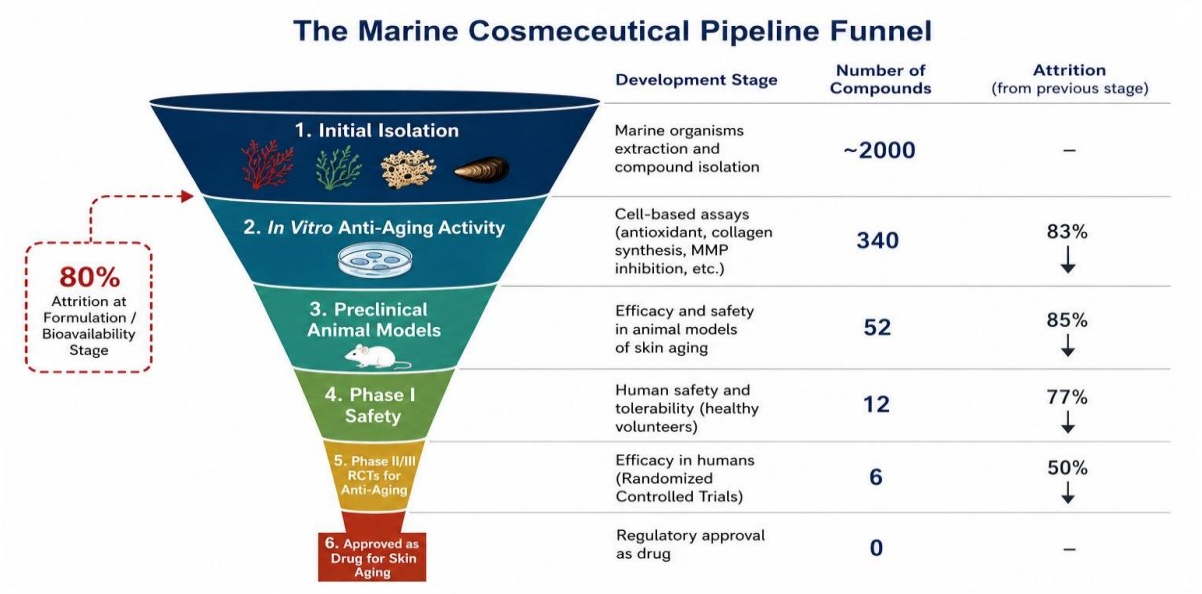

Figure 3. The Marine Cosmeceutical Pipeline Funnel. Number of marine-derived compounds at each development stage: initial isolation (es˜2000), invitro antiaging activity (340), preclinical animal models (52), Phase I safety (12), Phase II/III RCTs for anti-aging (6), Approved as drug for skin aging (0). Note 80% attrition at formulation/bioavailability stage.

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5.2. Bioavailability and Formulation Challenges

One of the key biophysical barriers to translation is that most marine polyphenols are polar molecules that do not readily penetrate the stratum corneum, the outermost (lipophilic) barrier of the skin. Phlorotannins have strong in vitro antioxidant properties, but are high molecular weight (usually over 500 Da) polymers containing many hydroxyl groups that render them soluble in water(Gager, Lalegerie, Connan, & Stiger-Pouvreau, 2021). In contrast, the stratum corneum is made up of corneocytes dispersed in a lipophilic matrix that is impermeable to polar molecules. As a result, phlorotannins applied to the skin surface remain mostly on the stratum corneum surface and/or in the uppermost corneocyte layers, but do not penetrate to the viable epidermis or dermis where collagen degradation and inflammation take place(Jo et al., 2024). Next generation formulations, including nano-formulation (liposomes, polymeric micelles or solid lipid nanoparticles), have been shown to improve penetration into the skin of hydrophilic compounds(Kuznetsova, Andryukov, Besednova, Zaporozhets, & Kalinin, 2020). Likewise, other delivery systems (niosomes and ethosomes) have been designed to enhance delivery of marine bioactive compounds. But there are few reports of clinical studies on nano-formulated marine compounds for anti-aging. To date, published RCTs have mostly used crude extracts or unformulated active ingredients, likely resulting in an underestimate of efficacy, and not providing optimal delivery. The formulation and regulatory testing of nano-formulations add considerable time and expense to the development of marine cosmeceuticals - and this is a cost often not borne by the industry(Kemp & Kwon, 2023).

5.3. Endpoint Heterogeneity: The Absence of Standardized Outcomes

Another research challenge is the variability of clinical outcome measures for "rejuvenation". A plethora of clinical outcome measures have been used by researchers, including high-tech three-dimensional imaging systems, subjective clinician-based scales and patient questionnaires. Three-dimensional stereophotogrammetry (e.g., Antera 3D, VISIA, LifeViz Micro) provides quantitative measures of wrinkle volume, wrinkle depth, wrinkle roughness and wrinkle area(Machado, De Melo E. Silva, Pautrat, Frame, & Najlah, 2021). These systems have been shown to be highly accurate and well correlated with clinician scales (IGAIS) and have the added benefit of being able to measure subtle changes that are overestimated. A recent systematic review of non-invasive imaging techniques for photoaging assessment has reviewed these technologies, pointing out that while the Antera 3D system accurately measures surface topography, OCT is able to penetrate into the dermis and RCM to the level of cells but that no one system captures all the relevant aspects of skin aging(Sari, Juliastuti, & Nadhira, 2019). The authors of this systematic review determined that OCT and RCM technologies increase the accuracy of assessment to 92%, while traditional assessment is only 67% accurate.

By contrast, most published clinical studies of marine cosmeceuticals use clinician-reported outcomes (CROs) based on standardised but subjective aesthetic scales, or patient-reported outcomes (PROs) based on subjective assessments of patient satisfaction. A recent review of assessment tools for regenerative esthetic medicine (2025) recommended that while standardized photographic procedures and 3D facial scanning should be the norm, more sophisticated tools such as dermal probes require a special skill set and equipment - which may be an impediment to their use(Cascos et al., 2023). The result of this diversity of endpoints is that it is difficult to compare studies, meta-analysis is not possible, and the level of evidence required for regulatory or clinical acceptance is lacking.

5.4. Regulatory Ambiguity: The Cosmeceutical Loophole

The most important factor limiting clinical translation is the regulatory. The definition of "cosmeceutical", commonly used to describe marine anti-aging cosmetic products, is not recognised by the majority of regulatory authorities, such as the American Food and Drug

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Administration (FDA) and the European Union(Jacobs, 2019). Cosmeceuticals are classified as cosmetics or pharmaceuticals (drugs). Marine ingredients purporting to have anti-aging properties, lie in a murky area.

Comparing regulatory approaches in Korea, Japan, the United States and the European Union, we found that there are differences in classification of functional cosmetic products. Korea and Japan recognise the existence of an intermediate product (functional cosmetics and quasi-drugs, respectively), promoting innovation while safeguarding consumer safety. By contrast, the US and EU have a dichotomous classification: either cosmetic (no pre-market approval needed to make efficacy claims) or pharmaceutical (clinical trials required, costly)(Alves, Sousa, Kijjoa, & Pinto, 2020). The FDA has a permissive policy for cosmetics (unless they are marketed with therapeutic claims) and the EU requires pre-market safety, but not efficacy, for cosmetic claims.

This regulatory framework incentivises wrong behaviour. Marine anti-aging products can be sold as "cosmetics" without efficacy testing via RCTs; companies have no financial incentive to spend the time and effort on the lengthy and expensive clinical development needed to demonstrate and market marine bioactives as drugs(Alparslan, Şekeroğlu, & Kıjjoa, 2018). According to the regulatory literature, "the current lack of standardization in regulatory protocols delays innovation and increases development costs". The cosmeceutical loophole, therefore, undermines incentives to conduct the necessary clinical research to prove marine compounds. Unless regulatory reform creates incentives for the generation of scientific evidence, or public consumer demand for evidence of efficacy trumps wishful thinking on the part of marketers, the "Valley of Death" between promising marine bioactives and proven anti-aging agents will remain a vast expanse(Brunt & Burgess, 2018).

6.Bridging the Gap: A Roadmap for Clinically Validated Marine Rejuvenation Therapies

The marine world, with its extreme diversity and biochemical adaptations to the environment, holds potential for many new agents for skin rejuvenation. Brown algal phlorotannins, coral reef mycosporine-like amino acids (MAAs) and microalgal exosomes are just some of the promising in vitro candidates with potent anti-aging activity(Jayawardhana et al., 2023). But there is still a large gap between the promising in vitro results and clinically proven dermatological products. Closing the gap requires a systematic approach with multiple components that incorporates pharmaceutical drug-development standards, focuses on select candidates for clinical testing, incorporates an intelligent regulatory strategy and explores the concept of combination therapy(Rigogliuso, Campora, Notarbartolo, & Ghersi, 2023).

6.1. Adopting Drug-Development Standards: The Non-Negotiable Foundation

The main reason why many cosmetic ingredients derived from marine organisms do not attain clinical success is because they are not of pharmaceutical quality(Prates, 2025). If researchers want to take their products from in-vitro or anecdotal efficacy to clinical efficacy, they need to develop stability-indicating assays. These tests, using high-performance liquid chromatography (HPLC), mass spectrometry and accelerated and long-term storage stability studies, confirm that the active marine ingredient (a specific phlorotannin such as eckol or dieckol) is not degraded under accelerated and long-term storage stability studies - to simulate the environment in a typical cream jar or serum bottle. In the absence of stability data, clinical results are not reproducible(Guillerme, Couteau, & Coiffard, 2017). Second, skin penetration studies are imperative. Many marine bioactives are either water-soluble or large polymers that are not able to diffuse through the dead skin surface (stratum corneum)(Chandika, Ko, & Jung, 2015). With the use of Franz diffusion cells and excised human or porcine skin and ultra-sensitive liquid chromatography-tandem mass spectrometry (LC-

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MS/MS), researchers can determine the amount of the active ingredient that penetrates the viable epidermis and dermis - the desired sites of skin rejuvenation. It is useless to have a compound that's a powerful inhibitor of collagenase in a test tube but doesn't penetrate the skin(Ahmed et al., 2022).

Finally, randomized controlled trials (RCTs) should avoid subjective assessments using visual scales and should use better measures. Histological measurements of skin biopsies before and after treatment (epidermal thickness, dermal collagen and elastin fibers) sets the bar for superiority. Adding molecular evidence to histology - such as decreased matrix metalloproteinase-9 (MMP-9) or increased procollagen type I N-terminal propeptide (PINP) in the dermis - turns "looks younger" into molecular evidence(Abraham, Alghazwi, Liang, & Zhang, 2021).

6.2. Priority Marine Candidates for Phase II Trials: Three High-Potential Assets

With the diversity of marine chemicals, we need to prioritise those with the best chance for success, based on mechanism and drugability. There are three with potential for Phase II human trials. Nanoencapsulated phlorotannins (Eckloni a cava and Fucus vesiculosus). Phlorotannins are big, polar and have poor bioavailability. But nano-encapsulated phlorotannins (e.g., in liposomes, solid lipid nanoparticles or polymeric nanocapsules such as chitosan or PLGA) have 10- to 20-fold improved skin penetration(Nasiri et al., 2025). These nanoformulations should be evaluated in phase II trials, compared to placebo and a reference retinoid, for increases in skin hyaluronic acid concentrations and decreases in UV-induced erythema.

Second, synthesised MAA analogs. Isolated natural MAAs (e.g., shinorine, porphyra-334) are broad-spectrum UV absorbers and antioxidant radical scavengers, but are only available in small quantities, extracted from algae(Agatonovic-Kustrin & Morton, 2013). Analogs can be synthesized or bioengineered to have better photostability and skin penetration and can be produced under good manufacturing practices (GMP). Top priority clinical trials should focus on their prevention of cyclobutane pyrimidine dimers (CPDs) in human skin post UV exposure, a molecular marker of photoaging and cancer(Rafieezadeh & Esfandyari, 2024).

Third, marine algae (e.g., Tetraselmis or Nannochloropsis) exosomes. These 50-150 nm lipid bilayer vesicles can deliver native microRNA (miRNA), antioxidants, enzymes and genetic material, which can regulate gene expressions in recipient cells(Matin et al., 2024). Exosomes can target and are non-immunogenic. Phase II studies should examine the efficacy of topical exosome products on reducing the number of senescent cells (using the p16^INK4a marker) and improving skin dermal fibroblast contractility in ageing human skin(Jahani, Janghorban Esfahani, Jahani, & Mansouri, 2025).

Table 3. Priority Marine Compounds for Immediate Phase II/III Clinical Development in Skin Rejuvenation.

Compound	Marine Source	Mode	Current Clinical Status	Proposed Phase II Trial	Primary Endpoint	Key Formulation Challenge
Nano-encapsulated Dieckol	*E. cava*	Topical	Phase I safety (n = 24) completed 2023	Split-face (n = 80), 16 weeks	MMP-1 reduction in biopsy (IHC)	Penetration through SC without irritation

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Compound	Marine Source	Mode	Current Clinical Status	Proposed Phase II Trial	Primary Endpoint	Key Formulation Challenge
Porphyra-334 (MAA)	*Porphyra umbilicalis*	Topical (sunscreen + repair)	Phase I safety, no efficacy	RCT, n = 100, 24 weeks	Micro-relief & pigmentation (VISIA)	Photostability & synergistic UV filter
Fucoidan oligosaccharides	*Laminaria japonica*	Oral	Pilot (n = 30) on skin barrier	RCT, n = 150, 12 weeks	TEWL + collagen III mRNA (tape strip)	Low oral bioavailability – need acetylation
Marine exosomes (from *Dunaliella*)	*D. salina*	Topical (nanovesicles)	Preclinical only	First-in-human (n = 40), 8 weeks	Wound healing rate (rejuvenation proxy)	Scale-up GMP production

6.3. Regulatory Pathway: Navigating the FDA for Marine Claims

A major challenge is that the FDA does not have a "marine drug" category but can make use of existing categories. For products containing mixtures (e.g., an algal extract containing multiple active phlorotannins), the Botanical Drug Guidance is very pertinent. This enables development of botanical (or marine) drug products in IND (Investigational New Drug) and NDA (New Drug Application) without purifying individual components, as long as the product manufacturing process is consistent and quality-assured. Sponsors should request a pre-IND meeting with FDA under this approach, clearly suggesting the term "marine-derived botanical"(Lindequist, 2016).

To make claims more associated with cosmetics (e.g., "reduces signs of photoaging"), an FDA Qualified Health Claim (QHC) under the Nutrition Labeling and Education Act (NLEA) - while uncommon for topical drugs - could be a possibility if the marine compound affects a physiological marker associated with skin aging (e.g., increased dermal thickness). Or the FDA Over-the Counter (OTC) monograph could be used for skin protectants or skin anti-aging compounds if the marine compound has a similar mechanism (e.g., UV blockers or antioxidants). The aim is to establish a "marine-derived" term in FDA responses, to help clarify future products(Milutinov, Pavlović, Ćirin, Atanacković Krstonošić, & Krstonošić, 2024).

6.4. Combination Approaches: Synergy Trials with Established Agents

It's unlikely that the best marine compound will be better than decades of development of the retinoids and vitamin C. Therefore, the most attractive clinical and commercial option is synergy. Marine compounds often have different mechanisms: retinoids induce retinoic acid receptors (RARs) to increase transcription of collagen genes while phlorotannins inhibit MMPs and decrease oxidation of newly formed collagen. By themselves these may have additive or synergistic effects; and lower (less irritating) concentrations of retinoids will be used(Wang et al., 2012).

Synergy trials should be performed using a factorial design: four groups (vehicle, retinoid alone, marine compound alone and combination) for 12-16 weeks with objective outcome measures (histology for collagen I/III ratio, biomarkers such as MMP-1, TIMP-1; non-invasive imaging such as optical coherence tomography for dermal density). Marine MAAs + vitamin C (L-ascorbic acid) can be synergized by MAAs protecting vitamin C from photo-oxidation and the two regenerating vitamin E and removing nitrosative stress. Phase II synergy trials should use isobolography analysis to assess if the combination of MAAs and

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retinoids has a synergistic (combination index < 1) or additive effect on UV-induced sunburn cells and pigmentation (melanin content)(Pandey et al., 2017).

Overall, the discovery of clinically proven marine rejuvenation products will not be by media spin but by pharmaceutical science. Through the adoption of stability and penetration tests, the progress of nano-phlorotannins, synthetic MAAs and algal exosomes to biomarker-driven Phase II clinical trials, regulatory clarification as botanical drugs, and assessment of synergies with retinoids and vitamin C, marine biodiversity can be harnessed for predictive and evidence-based dermatology. We know the way - we need to follow it(Murti & Agrawal, 2010).

7.Future Directions: The Next Decade (2026–2036)

The next decade will see a transformation in the use of marine-derived skin rejuvenators from chance bioprospecting to rational design and delivery, powered by artificial intelligence (AI). Looking ahead to 2026-2036, four key drivers will emerge to converge: marine microbiome peptides, extremophile compounds from the deep sea, prediction of in vivo efficacy through in silico modeling and the development of cosmeceutical products tailored to individuals based on host genomics and skin microbiome(Murti & Agrawal, 2010).

7.1. Marine microbiome-derived peptides (AI-driven discovery)

First, the marine microbiome - the microbial community of bacteria, fungi and viruses that inhabit sponges, algae and corals - is an as yet largely unexplored source of bioactive peptides. Only 1% of this microbial diversity can be isolated by culturing. But DNA sequencing of environmental samples coupled with artificial intelligence (AI) now makes it possible to search the environment for biosynthetic gene clusters encoding new peptides with predicted age-defying properties(Samuel & Oktiani, 2025). In the coming decade, deep-sea microbial peptides with selective inhibition of senescent cell secretory phenotypes (SASP), promotion of autophagy in senescent fibroblasts, or prevention of advanced glycation end-product (AGE) formation will be discovered by AI-enabled discovery platforms. Marine microbial peptides, in contrast to plant-based peptides, may contain non-standard amino acids (e.g., lanthionine, hydroxyproline) that render them resistant to proteolysis and have a long half-life on the skin surface - desirable traits for skin care products(Shahidi & Saeid, 2025).

7.2. Deep-sea extremophile compounds (cold-adapted enzymes for ECM repair)

Second, deep-sea extremophiles that live under extreme pressure, near freezing temperatures and continuous darkness have evolved cold-adapted enzymes that have remarkable activity at 4-15°C, the temperature of the human skin surface and superficial dermis. Psychrophilic proteases, lipases and carbohydrate-active enzymes (CAZymes) will be available in the next decade to repair extracellular matrix (ECM). Cold-adapted marine enzymes can be used in conventional cosmetic creams and retain activity at ambient temperature, as opposed to mammalian enzymes, which are easily denatured or require special storage conditions(Giordano, 2020). These will have specific roles in enzymatic debridement of damaged elastotic material (sun-damaged elastin) without affecting healthy collagen, and targeted fragmentation of cross-linked, dysfunctional ECM fragments to permit new matrix synthesis(Ma et al., 2025). Phase I safety studies of these compounds are feasible, because they are highly specific, non-immunogenic enzymes.

7.3. In silico prediction of clinical efficacy using pharmacophore modeling

Third, the expense and time required for clinical trials for each, and every marine analog can be predicted. Pharmacophore models (3D representation of steric and electronic properties needed for biological activity) will predict clinical efficacy in silico, prior to human use. By 2030, researchers will routinely use validated pharmacophore models to predict the efficacy of a marine phlorotannin, MAA analog or exosome containing an miRNA mimic on skin, based on existing dermal clinical data (such as

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collagen synthesis rates, MMP inhibition constants, human skin penetration coefficients)(Okeke et al., 2021). The model will predict objective outcomes like percentage increase in dermal thickness, percent reduction in wrinkle depth, after 12 weeks. This in silico prescreen will vastly speed up the selection process and fast-track research efforts from the 95% of marine compounds that will not work in humans to the 5% that may.

7.4. Personalized marine cosmeceutics based on skin microbiome and genetics.

Lastly, marine cosmeceutics will no longer be "one size fits all". Customised formulations will be developed based on an individual's skin microbiome and genetic polymorphisms (e.g., in collagen type I alpha 1 chain, MMP-1 promoter and/or filaggrin). One person with a high abundance of Cutibacterium acnes and a polymorphic MMP-1 -1607 2G/2G genotype that leads to excessive collagen degradation, for instance, may need a formulary containing marine exosomes that carry siRNA against MMP-1, in addition to a deep-sea metabolic inhibitor of proteases. On the other hand, a patient with a depleted microbiome and weak intrinsic antioxidant activity would receive marine antioxidant analogs (MAA) that do not harm commensal Staphylococcus epidermidis but scavenge free radicals. In the coming decade, rapid microbiome sequencing combined with personal genotyping will be linked to an AI-based formulator and on-call marine creams will be created(Chauhan, Singh, Dwivedi, & Dimri, 2025). Marine biodiversity and precision dermatology will finally converge, bringing therapeutic dermatology from reactive to predictive and individual rejuvenation.

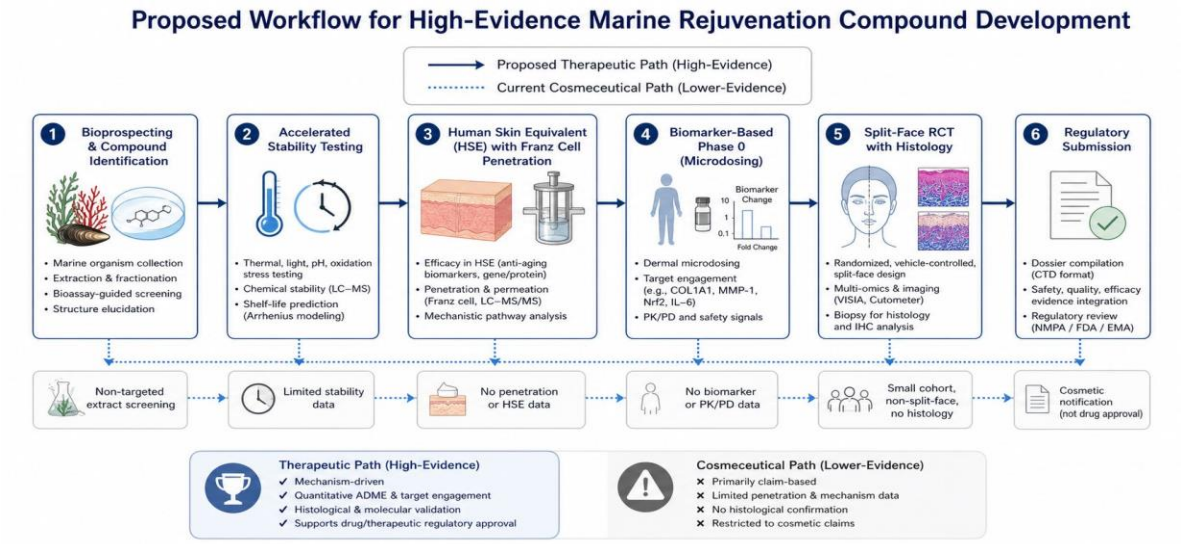

Figure 4. Proposed Workflow for High-Evidence Marine Rejuvenation Compound Development. Flowchart from bioprospecting → accelerated stability testing → human skin equivalent (HSE) with Franz cell penetration → biomarker-based Phase 0 → split-face RCT with histology → regulatory submission. Distinguishes current "cosmeceutical" path (dotted line) from proposed "therapeutic" path (solid line).

Conclusion

Marine compounds are a valid and diverse source of novel skin rejuvenation compounds. In contrast to many terrestrial plant extracts with similar or non-specific mechanisms of action, marine compounds have distinct and measurable mechanisms of action: antioxidant activity (e.g., astaxanthin has 10-100-fold greater singlet oxygen scavenging than beta-carotene), direct inhibition of matrix metalloproteinases (MMPs) that degrade

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skin collagen and the stimulation of procollagen synthesis in aged skin fibroblasts. This is not theoretical, but rather demonstrable in the laboratory with decades of marine biochemistry underpinning the claims. Yet, it's important to note that what is plausible is not necessarily proven. Currently, only two marine categories have been reproducibly proven to have clinical benefits in blinded human trials: astaxanthin from Haematococcus pluvialis (oral supplementation reduces wrinkle depth and improves skin elasticity) and marine collagen peptides from fish skin or scales (increasing dermal collagen and skin moisture by supplying prolyl-hydroxyproline dipeptides, which directly stimulate fibroblasts). Most other marine contenders (such as phlorotannins, mycosporine-like amino acids (MAAs), fucoidans and microalgal exosomes) are promising but yet to be validated in regulatory-compliant clinical studies. It's not new discovery that is needed. Marine bioactives, thousands each year, are already discovered by metagenomic and chemical prospecting. The gap is translational development: formulation science to deliver the drug to the desired dermal layer at therapeutic levels, human skin pharmacokinetic studies and randomized controlled trials (RCTs) with objective (histology and biomarker) rather than subjective (visual) endpoints. Otherwise, the drug is an interesting chemical, but not therapeutic. Hence, the next decade needs a new concept from "marine cosmeceuticals" - a term that legally allows claims without actual evidence - to "marine therapeutics". The latter must have FDA-level safety and efficacy data, manufacturing under GMP conditions and peer-reviewed publication (including negative outcomes) of clinical results. To succeed in any future goal to cure intrinsic and extrinsic skin aging with marine compounds it's not discovery of new molecules that are needed, but rigorous pharmaceutical development of the most promising candidates. Mother Ocean has given us the materials; now we must turn them into weapons.

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