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Review Article

The promise of marine molecules as cosmetic active ingredients

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Abstract

The marine environment represents an underexploited resource for the discovery of novel products, despite its high level of biological and chemical diversity. With increasing awareness of the harmful effects of chronic ultraviolet exposure, and a universal desire to improve cosmetic appearance, the market for new cosmetic ingredients is growing, and current trends have generated a greater demand for products sourced from the environment. A growing number of novel molecules from marine flora and fauna exhibit potent and effective dermatological activities. Secondary metabolites isolated from macroalgae, including carotenoids and polyphenols, have demonstrated antioxidant, anti-ageing and anti-inflammatory activities. In addition, marine extremophilic bacteria have recently been shown to produce bioactive exopolymeric molecules, some of which have been commercialized. Available data on their activities show significant antioxidant, moisturizing and anti-ageing activities, but a more focussed investigation into their mechanisms and applications is required. This review surveys the reported biological activities of an emerging and growing portfolio of marine molecules that show promise in the treatment of cosmetic skin problems including ultraviolet damage, ageing and cutaneous dryness.

Résumé

L'environnement marin représente une ressource sous-exploitée pour la découverte de nouveaux produits, malgré son niveau élevé de diversité biologique et chimique. Avec la prise de conscience croissante des effets néfastes de l'exposition chronique aux ultraviolets et un désir universel d'améliorer l'apparence, le marché des nouveaux ingrédients cosmétiques est en croissance et les tendances actuelles ont généré une plus grande demande pour les produits issus de l'environnement. Un nombre croissant de nouvelles molécules issues de la flore et de la faune marines présentent des activités dermatologiques efficaces et performantes. Les métabolites secondaires isolés des macroalgues, y compris les caroténoïdes et les polyphénols, ont démontré des activités antioxydantes, anti-vieillissement et anti-inflammatoires. De plus, il a été démontré récemment que les bactéries extrêmophiles marines produisent des molécules exopolymériques bioactives, dont certaines ont été commercialisées. Les données disponibles sur leurs activités montrent des activités antioxydantes, hydratantes et anti-ages significatives, mais une investigation plus ciblée de leurs mécanismes et applications est requise. Cette revue étudie les activités biologiques rapportées d'une gamme émergente et croissante de molécules marines prometteuses, dans le traitement des problèmes de peau cosmétiques, y compris les dommages causés par les ultraviolets, le vieillissement et la sécheresse cutanée.

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Introduction

Increasing antibiotic resistance and incidence of infectious disease is a serious and growing concern [1–4]. Crucially, the skin offers a primary barrier to infection [5] by providing a semi-permeable surface allowing the passage of materials into and out of the body. The skin also provides a barrier to excessive water loss [6–8], which is important in maintaining tissue hydration as well as cutaneous health. Should this primary barrier become compromised, the body may be more susceptible to infection; therefore, preserving the health, integrity and function of the skin is vital.

However, maintaining healthy skin is problematic due to several damaging factors, which can lead to cosmetic issues that affect the overall complexion of the skin. Wrinkles, skin laxity, abnormal pigmentation and skin dryness can be artefacts of harmful oxidative molecules that originate internally and externally, and may become more apparent with age. In youthful skin, dryness is generally caused by low humidity, leading to failure of normal desquamation and disrupted production of the natural moisturizing factor of the stratum corneum [9], whereas an ageing-related reduction in integral dermal skin matrix molecules further contributes to laxity and dryness [10, 11]. Thus, there is a growing and unmet need for new cosmetic active ingredients that can alleviate these problems.

Increasingly, the analysis and characterization of active substances from biologically derived materials, in particular plant-derived substances, are being reported [12–15]. The marine environment is also being recognized as a promising source of cosmetic ingredients, due to its unrivalled biological and chemical diversity [16–18].

Several bioactive molecules from marine organisms have been shown to enhance the cosmetic appearance of skin through antioxidative, moisturizing and anti-ageing actions. This review discusses the current applications and prospects for marine-derived molecules in cosmetic applications.

Photoprotective molecules

Increased awareness of the harmful effects of ultraviolet radiation (UVR) has generated a greater demand for photoprotective products. Chronic exposure to UVR is known to cause skin cancer, photo-ageing and sunburn [19–23]. UVA and UVB can damage skin cell DNA [24, 25], increasing the risk of skin cancers via gene mutations [20, 26] and immunosuppression [21, 27]. Although the best way of avoiding UV damage is to avoid sunlight, this is not always feasible. Frequent use of antioxidant UV protectants is essential to lessen skin damage; otherwise, treatments exist to combat the resulting skin problems associated with excessive UV exposure.

The term 'antioxidant' encompasses a broad range of molecules with several activities, including photoprotection, and scavenging/immobilizing of reactive oxygen species (ROS), thus preventing oxidative damage to cell components. As the body ages, its ability to regulate ROS decreases, whereas the production of mitochondrial ROS increases [28], meaning tissues are more susceptible to oxidative stress with age. Several antioxidants exist in the pharmaceutical, cosmetic and food industries, including the marine exopolysaccharide (EPS) deepsane. Deepsane was isolated from the deep-sea marine bacterium *Alteromonas macleodii*, from a hydrothermal vent polychaete *Alvinella pompejana*, close to the East Pacific rise at 2600 m [29]. Two oligosaccharides within the EPS were found to protect epidermal keratinocytes and Langerhans cells from inflammatory mediators, including UVR [30]. Deepsane has been marketed as Abyssine® by Lucas Meyers as the first commercialized marine EPS [12, 31]. The chemical structure of this unusual polysaccharide has also been reported [32]. It contains, for example, an unusual trisubstituted galacturonic acid and represents one of the most complex carbohydrate structures so far reported. It was found to contain seven types of monosaccharides, with considerable variability of the repeating unit [32]. Progress towards its full chemical structure determination and analysis of its constituent oligosaccharide components will add in developing a mechanistic understanding of its cosmetic activities. This exciting discovery highlights the great chemical complexity that exists in the marine environment, with extremophilic bacteria offering a platform for the future discovery of new cosmetic molecules with novel structures and functions.

Several other marine molecules (summarized in Table I.) including mycosporine-like amino acids [33–36], carotenoids [37–39] and polyphenols [40–46] have also shown antioxidant activity.

Mycosporine-like amino acids

Mycosporine-like amino acids (MAAs) are protective secondary metabolites commonly produced by marine organisms under high UV stress, including cyanobacteria, macro- and microalgae [47, 48]. These compounds absorb UVR of 310-360 nm [49] and avoid the production of ROS by dissipating the absorbed energy as heat [49–51]. Karentz *et al.* [52] hypothesized that Antarctic organisms produce biological sunscreens due to ozone-related increases in UVR levels [53–55]. Fifty-seven species were collected, including fish, algae and invertebrates, 90% of which contained MAAs. It was highlighted that whereas plants are known to synthesize MAAs, marine animals bioaccumulate MAAs from their diet; therefore, their exploration as UV protectants may be better focussed on marine algae, where high MAA content has been frequently reported in the Rhodophyta [56–59]. In particular, MAAs containing mycosporine-glycine: valine have shown most promise as antioxidants as they can scavenge superoxide anions [33, 36] and impede lipid peroxidation [34, 35], which otherwise promotes membrane lipid damage [60, 61]. Despite these potent activities, few MAAs have reached the cosmetic market, due to high reactivity and instability [62]. Cosmetic formulations containing MAAs (porphyra-334, shinorine and palythine), isolated from the rhodophyte *Porphyra umbilicalis*, have reached the cosmetics market under the trade names Helionori® and Helioguard 365® [63]. Some peer-reviewed data have been published on their actions, suggesting photoprotective and anti-ageing properties [64], and some commercial literature has also been reported. However, more robust biochemical data are needed to understand the underlying mechanisms of action.

Carotenoids

The inhibition of lipid peroxidation is also a function of carotenoids. Shimidzu *et al.* [37] isolated several carotenoids from various marine organisms which exhibited 40-600 times greater antioxidant activity against the superoxide anion producer 1,4-dimethylnaphthalene, than the commercially available antioxidant α-tocopherol. Similarly, the carotenoid fucoxanthin, extracted from the phaeophyte *Undaria pinnatifida*, has shown 13 times greater scavenging ability of hydroxyl radicals ($HO^{\bullet}$) than α-tocopherol [38]. In addition, marine-derived carotenoids astaxanthin, zeaxanthin, fucoxanthin, β-carotene and lutein, have exhibited potent ROS scavenging activity *in vivo* [39], greater than that of known antioxidants. Astaxanthin was 94 times more effective at scavenging hypochlorous acid (HOCl) than both α-tocopherol. Zeaxanthin and lutein were also highly effective at scavenging HOCl which act in accord with ROS to cause oxidative stress to cell components [65].

Despite these data suggesting that several marine carotenoids are efficient antioxidants, few are present in topical cosmetics or sunscreens, due to a lack of promising data from *in vivo* trials. Oral supplements containing marine antioxidants to improve skin health have scarcely reached the cosmetic market due to their low bioavailability [66]. The absorption efficiency and biocompatibility of marine carotenoids on the skin are yet to be determined and will be crucial in understanding their true potential as antioxidant sunscreen ingredients.

Polyphenolic compounds

It has been recognized for several decades that polyphenols from terrestrial plants have antioxidant properties [67]. More recently, marine plants have been highlighted as a viable source of unique polyphenolic antioxidants, due to their easy production and maintenance [68]. Polyphenols are aromatic secondary metabolites derived from plants with benzene ring structures attached to at least one polyphenolic hydroxyl group (Fig. 1) and encompass flavonoids and tannins [41]. Polyphenolic extracts containing flavonoids and tannins from the halophytes *Lithrum salicaria*, *Frankenia pulverulenta*, *Pistacia lentiscus* and *F. laevis*, are suggested to have significant antioxidant activities [69]. During *in vitro* radical scavenging and metal chelation assays, these polyphenolic extracts were effective at low concentrations allowing 50% of maximal oxidative inhibition (ranging from 0.03 to 0.50 mg mL^{-1}), in free radical solutions [69]. Ferrous iron (Fe^{2+}) is able to transfer single electrons to hydrogen peroxide to form $HO^{\bullet}$ [40, 70]; therefore, its chelation is considered a promising route in the inhibition of free radical activity [71]. It has, however, been reported that some

Table I The marine molecules, their sources, actions and limitations explored in this review.

Molecule class	Bioactive molecule(s)	Source(s)	Action(s)	Type of data presented	Limitation(s)	References
			Ultraviolet damage			
Mycosporine-like amino acids	Mycosporine-glycine:valine	*Palythoa tuberculosa*, *Porphyra tenera*, *Lissoclinum patella*	Antioxidant: lipid peroxidation, radical scavenging, antibacterial	*In vitro*	High reactivity, instability [62]	[33–36]
	Porphyra-334, shionine, palythine	*Porphyra umbilicalis*	Antioxidant: photoprotection, antiaging	Commercialised (Helionori®, Helioguard 365®)	N/A	[57, 64]
	13-*O*-(β-galactosyl)-porphyra-334	*Nostoc sphaericum*	Antioxidant: radical scavenging, UV protective	*In vitro*	Preliminary data	[36]
Carotenoids	Astaxanthin, zeaxanthin, lutein/lutein B, Tunaxanthin, Halocynthiaxanthin, fucoxanthin, β-carotene	*Agrobacterium auranitiacum*, *Haematococcus pluvalis*, *Pneuoatophorus japonicas*, *Oncorhynchus mykiss*, *Sehola quinqueradiata*, *Undaria pinnatifida*	Antioxidant: radical scavenging	*In vitro*, some *in vivo*	Mostly *in vitro* data, low bioavailability [66], unclear origins of molecules in *in vivo* trials [39]. Some commercialised oral supplements	[37–39]
Polyphenols compounds	Unspecified flavonoids/ tannins	*Lithrum salicaria*, *Frankenia pulverulenta*, *Pistacia lentiscus*, *F. laevis*	Antioxidant: radical scavenging, metal chelation	*In vitro*	Potential cytotoxicity [71]	[69]
	Phlorotannins: diphlorethol, triphloroethol, trifuhalol and tetrafuhalol, phloroglucinol, eckol, eckstolonol	*Halidrys siliquosa*, *Ecklonia cava*, *Ascoseira mirabilis*, *Cystosphaera jacquinotii*, *Ishige okamurae*	Antioxidant: UV protective, radical scavenging	*In vitro*, some *in vivo*	Mostly *in vitro* studies, *in vivo* study conducted on zebrafish [45] – dissimilar to humans, more interest in anti-cancer actions	[42–46, 79]
			Hyperpigmentation			
Polyphenols compounds	Unspecified flavonoids and tannins, phlorotannins: phloroglucinol, eckstolonol, eckol, phlorofucofuroeckol, dieckol	*Sargassum polycystum*, *Ecklonia stolonifera*, *E. cava*, *S. silquastrum*	Tyrosinase inhibition, anti-melanogenesis	*In vitro*, some *in vivo*	Cytotoxicity [97], some studies use unreliable testing methods, *in vivo* study conducted on zebrafish [45] – dissimilar to humans, more interest in anticancer actions	[97–99]
	Unspecified flavonoids and tannins	*Pistacia lentiscus*	Tyrosinase inhibition	*In vitro*	Preliminary data, yet to be confirmed *in vivo*	[69]
	Sulphated flavonoid: luteolin 7-sulphate	*Phyllospadix iwatensis*			Preliminary data	[101]
Polysaccharides	Sulphated polysaccharide: fucoidan	*Fucus vesiculosus*	Indirect anti-melanogenesis	*In vitro*	Trials on non-human cells	[103, 104]
			Aging			
Proteins and peptides	Marine collagen	Fish skin/bone, echinoderm tests, cnidarians, cephalopods	Alternative to terrestrial collagen	N/A	Not hailed as antiaging remedy, terrestrial collagen unclear antiaging mechanism	[127–135]
	Unspecified serine endo-protease, oleic acid, linoleic acid	*Salmo salar*	Wrinkle reduction, anti-erythema, pigment correction, skin hydration	Commercialised: Zonase enzyme	N/A	[141]
	Tripeptide containing arginine-glycine-aspartic acid	*Ulva lactuca*	Induced collagen 1 synthesis via TGF-p pathway	*In vitro*	Lack of recent literature	[151]
	Unspecified peptide extracts	*Chlorella vulgaris*, *Ulva pertusa*	Reduced expression of MfvIP-1, induced collagen I synthesis	*In vitro*	Lack of recent literature	[145, 146]

Table I (continued)

Molecule class	Bioactive molecule(s)	Source(s)	Action(s)	Type of data presented	Limitation(s)	References
Polysaccharides	Sulphated polysaccharide: fucoidan	*Undaria pinnatifida*, *Fucus vesiculosus*	Collagenase and elastase inhibition, SIRT1 upregulation	Few *in vitro* and *in vivo* trials	*In vivo* trials less significant	[139, 140]
Carotenoids	Astaxanthin	*Haematococcus pluvialis*, *Euphausia superba*	Decreased TEWL, wrinkle reduction, improved elasticity, skin hydration, improved age spots, murine MMP-13 suppression	Clinical trials, *in vivo* (murine)	Majority of literature from one research group, mechanism of action not clear in human trials	[147–153]
			Dry skin			
Fatty acids	Omega-3 and -6 oils, EPA, DHA	Several species of marine and freshwater fish, *Loligo loligo*	Reduced irritation and TEWL, skin hydration	*In vivo* (murine)	Not trialled as topical treatment	[164–167, 173]
	Fish oil wax ester containing fatty alcohols/acids	*Hoplostethus atlanticus*	Skin hydration	Clinical	*H. atlanticus* vulnerable to exploitation [172]	[170]
Proteins	Marine collagen	*Nemopilema nomurai*, *Chondrosia reniformis*	Moisturising, increased skin lipid content	*In vitro*	Preliminary data, prospective outcomes, insolubility [116]	[121, 182]
Polysaccharides	Bacterial EPS	*Polaribacter* sp. SM1127, *Phyllobacterium* sp.	Water absorption, humectant	N/A	No *in vivo* or *in vitro* data available	[195, 196]
		Vibrio diabolicus	Stimulated HA synthesis and fibroblast proliferation, skin hydration, neuronal exocytosis inhibition	*In vitro*	Only patent literature available	[197]
		Unspecified marine bacteria	Antiaging, moisturising	Commercialised: (Hyanify™, Hyadisine®)	No supporting literature	[198, 199]

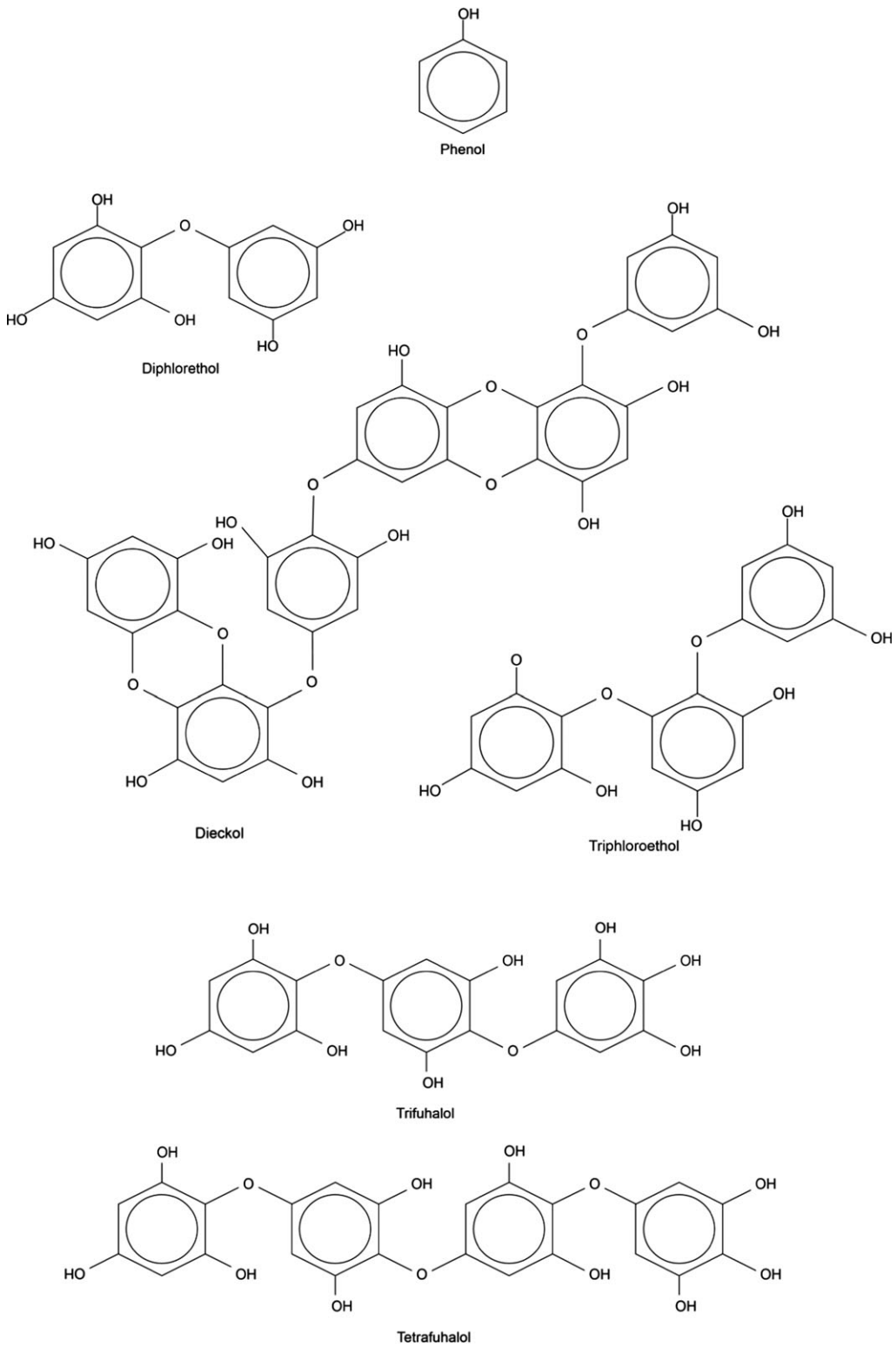

Figure 1 Chemical structures of a simple phenol and polyphenol phlorotannins. Phlorethols: diphlorethol and triphloroethol, eckol: dieckol, and fuhalols: trifuhalol and tetrafuhalol. The fuhalol structures shown here are the A isomers.

metal chelators show cytotoxicity [71], and several plant-derived antioxidants have been shown to cause allergic reactions [72, 73]; thus, the safety profile of these extracts would need to be determined *in vivo* to determine their commercial viability.

Marine algae have been shown to produce polyphenolic compounds collectively known as phlorotannins, which have unique chemical structures (Fig. 1) due to the extreme environments in which they are found [74–76]. These compounds are thought to make efficient antioxidants due to the large number of hydroxyl groups present in their structures (Fig. 1), capable of donating protons [77, 78]. Recently, novel extracts from the phaeophyte *Halidrys siliquosa* containing phlorotannins diphlorethol, triphloroethol, trifuhalol and tetrafuhalol, showed their radical/superoxide scavenging ability was positively correlated with the total phenolic content of the extract [44]. Other phaeophyte phlorotannins have been reported to show UV screening [43, 79], cellular damage reduction [80], ROS scavenging [42, 43] and antioxidative effects [45, 46], with most cosmetic interest from *Ecklonia cava* phlorotannins.

Overall, it can be concluded that marine antioxidants show promise in the prevention of UV-related skin damage. Nevertheless, there is a surprising lack of their incorporation into skin products. This may be due to greater interest in marine antioxidants as anticancer molecules [67] than for UV protection, as this is considered a more crucial avenue of antioxidant research. Several of the explored antioxidants have dual cosmetic function, such as polyphenolic compounds which have exhibited antioxidant, antibacterial, anti-pigmentation and anti-ageing activities [44, 81, 82]; therefore, the current knowledge is essential to progress to *in vivo* trialling and for the development of these compounds as new cosmetic ingredients.

Anti-pigmentation molecules

Hyperpigmentation is a common symptom of ageing and chronic ultraviolet (UV) exposure, often appearing as abnormal brown patches of skin, particularly in areas frequently exposed to the sun [83, 84]. The production of melanin occurs in the melanocytes of the epidermis via a series of oxidation reactions, catalysed by metalloenzyme oxidase: tyrosinase. Tyrosinase catalyses the conversion of L-tyrosine to dihydroxyphenylalanine (DOPA) and the conversion of DOPA to quinone [85, 86] – two important steps in melanin synthesis that limit the rate of production. As the body ages, the distribution of DOPA-positive melanocytes becomes less even as their frequency decreases [83, 87], meaning remaining areas of high melanocyte density are likely sites of discoloured skin. Consequently, a common route of hyperpigmentation treatment is via the inhibition of tyrosinase [88]. Current topical inhibitors: hydroquinone (HQ) – a phenol – and kojic acid (KA) [89] have been reported to cause irritation, erythema and contact dermatitis [90–94]; therefore, alternative tyrosinase inhibitors are being explored [95], with the skin-whitening industry predicted to be worth USD 23 billion by 2020 [96].

Polyphenolic tyrosinase inhibitors derived from marine plants and algae have shown moderate success [95]. Phlorotannins from the phaeophyte *Sargassum polycystum* have shown potent anti-melanogenesis/skin-whitening effects in both cell-free mushroom and cellular tyrosinase assays [97]. Tyrosinase activity and melanogenesis were inhibited in murine B16F10 melanoma cells, comparable to KA, and the extract displayed cytotoxicity at doses greater than 100 μg mL^{-1}, although this may not represent its cytotoxicity profile in human cells. This is consistent with similar studies on the activities of polyphenolic extracts from other phaeophytes: *Ecklonia stolonifera*, *E. cava* and *S. silquastrum* [98, 99]. Phlorotannin dieckol, extracted from *E. stolonifera*, has shown anti-tyrosinase activity three times that of KA [95]. It is thought that cellular tyrosinase assays produce more reliable results than cell-free tyrosinase assays, due to differences in the origins of plant and animal cell tyrosinases [97]. Therefore, results obtained from mushroom tyrosinase assays [98, 99] may not be analogous to human cell equivalents and should be cautiously interpreted.

Recently, other marine plants and their polyphenolic compounds have been identified as potential tyrosinase inhibitors, in assays using human cell lines. Lopes *et al.* [69] demonstrated the inhibition of tyrosinase on both human and murine cells, using phenolic extracts containing flavonoids and tannins from the halophyte *Pistacia lentiscus*. It was thought that the high concentrations of flavonoids within its leaves are responsible for its anti-tyrosinase action [100], showing potential in the treatment of pigment-related issues; however, this is yet to be confirmed *in vivo*. Similarly, phenolic extracts from 50 marine algae have been shown to inhibit tyrosinase activity of human epidermal melanocytes [101]. The most effective tyrosinase inhibitor was the sulphated flavonoid luteolin 7-sulphate (Fig. 2), isolated from the seagrass *Phyllospadix iwatensis*, which showed up to 100% greater inhibition than commercial inhibitor arbutin, in addition to low cytotoxicity. It is reported that compounds which possess a 4-substituted resorcinol skeleton (highlighted in Fig. 2) exhibit great tyrosinase inhibition as this region competes for DL-DOPA inhibition [102], leading to decreased melanin production. This highlights a promising foundation of anti-melanogenesis research, where several polyphenols and flavonoids are emerging as novel cosmetic and pharmaceutical ingredients, but mainly as antioxidants and photoprotectants [83, 84].

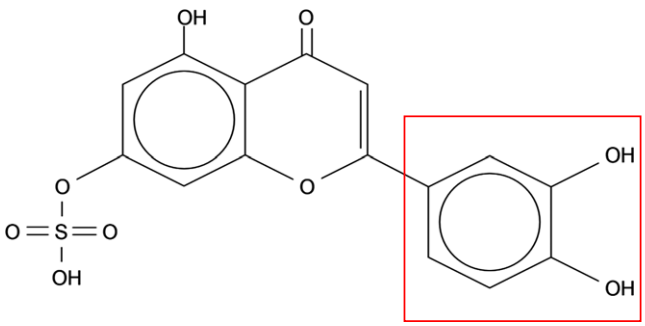

Figure 2 Chemical structure of the sulphated flavonoid, luteolin 7-sulphate. The active 4-substituted resorcinol region is highlighted.

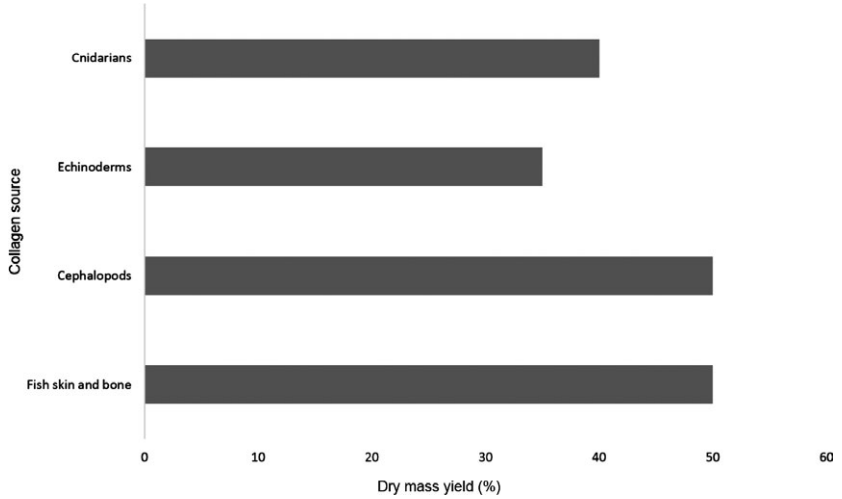

Figure 3 Approximate dry mass yields of collagen from different marine sources; fish skin and bone [127–130], cephalopods [134, 135], echinoderm tests [131] and cnidarians [132, 133].

Fucoidan, also a phaeophyte secondary metabolite, has been documented as a potential anti-pigment treatment, with evidence for its mechanism of indirect melanogenesis inhibition [103, 104], but has not yet been pursued as a cosmetic ingredient. Song *et al.* [103] reported that this sulphated polysaccharide from phaeophyte *Fucus vesiculosus* downregulated melanin synthesis via the activation of the extracellular signal-related kinase (ERK) pathway, which has been shown to cause the degradation of microphthalmia-associated transcription factor [105] – which is involved in melanin production [106]. This was shown using Mel-Ab cells – a murine melanocyte cell line which is particularly efficient in producing melanin [107]. The addition of potent ERK inhibitor PD98059 caused the resumption of melanin production, illuminating the anti-melanogenesis mechanism of fucoidan. Like the previous studies [97–99], *in vitro* assays were conducted on non-human cells; thus, the effect of fucoidan as an anti-pigment treatment is yet to be determined in human trials.

Although the cosmetic treatment of hyperpigmentation using marine molecules has been explored, the data are preliminary. Other cosmetic and ageing-related issues, such as wrinkles, loss of elasticity and dry skin, are considered to have a broader impact; for example, two-thirds of cosmetic sales were attributed to anti-ageing and moisturizing products in 2012 [108].

Anti-ageing molecules

With ever-increasing life expectancies in several countries around the world, the physical appearance of ageing is becoming an increasingly common cosmetic issue [109]. Ageing is generally associated with the formation of wrinkles, skin laxity, and hyperpigmentation [110–112] and can commonly be classed as long-term damage from various stressors. Damage to dermal cellular proteins, responsible for the synthesis of structural components, can lead to the propagation of these characteristics associated with ageing [113, 114]. Whereas the aforementioned antioxidants may delay the appearance of ageing, other treatments exist to lessen the symptoms of aged skin (Table I.), for example wrinkle reduction, increased cutaneous hydration and collagen replenishment, where chronological ageing may be caused by the slowing of cellular processes [113, 115] and the resulting progressive loss of key dermal skin matrix molecules such as collagen and hyaluronic acid [10, 11, 116].

Collagen

Despite the crucial role of collagen as a structural skin protein, its efficiency as an active ingredient in topical moisturizers is not well supported. Terrestrial collagen and its derivatives have been shown to induce keratinocyte proliferation *in vitro* [117, 118], and reduce UVB photo-ageing [119], increase dermal fibroblast density and improve collagen fibril structure [120] as oral supplements *in vivo*. Interestingly, the use of collagen from marine sources in cosmetic products is increasing [12, 121–126]. Large quantities of collagen have been extracted from marine biomass (Fig. 3) [127–135]. In addition, biocompatibility studies have shown that marine collagen exhibits lower cytotoxicity and greater cell viability than bovine collagen in tissue engineering assays [126]. Although not directly linked to cosmetic applications, this demonstrated biocompatibility suggests that the cosmetic applications of marine collagen are likely to grow in the future.

Available scientific data on topical collagen anti-ageing effects are negligible, which is surprising considering its widespread application in several products [136]. Therefore, the aim of future cosmetic collagen research should be based upon understanding its mechanisms as an anti-ageing ingredient, where the available data on marine collagen extraction provide good preliminary data on potential collagen sources.

Alternatively, the inhibition of the degradative enzymes, collagenase and elastase, can counteract the process of ageing. This has been demonstrated successfully using several terrestrial plant extracts [137, 138], but marine sources have received less attention. Recently, sulphated polysaccharide fucoidan was obtained from the phaeophyte *Undaria pinnatifida* and was shown to inhibit bacterial collagenase and human neutrophil elastase *in vitro* [139]. Additionally, a polyphenolic extract, containing fucoidan from the

phaeophyte *Fucus vesiculosus*, showed significant inhibition of elastase *in vitro* [140]. Further *in vitro* assays showed that both extracts upregulated the *SIRT1* protein, which causes the skin to appear more youthful by catalysing the breakdown of sugars and lipids [140]. Despite this success, it was noted that these results may not represent the true effects achieved in clinical trials, of which initial results were less significant *in vivo*.

Enzymes and peptides

A novel enzyme isolated from the eggs of Atlantic salmon, *Salmo salar* has been explored as a skin rejuvenation/anti-ageing ingredient [141]. The serine endoprotease (named Zonase) is used to break down the eggshell during hatching, leaving the embryo intact. It is also shown to be capable of enzymatic exfoliation of dead keratinocytes whilst stimulating new skin cells to grow. Lønne *et al.* [141] demonstrated that topical application of *S. salar* egg extract promoted wrinkle reduction, anti-erythema, even pigmentation and improved cutaneous hydration, without any adverse side effects. The extract contained unsaturated fatty acids, proteins, DNA, RNA, vitamins and minerals. It was speculated that the fatty acids (e.g. oleic acid and linoleic acid) increased transdermal absorption, allowing active ingredients to penetrate the dermis. The anti-wrinkle activity was the most potent effect observed and was hypothesized to be an effect of vitamin A, amino acids, zinc and copper, which aid in maintaining skin elasticity and structure of the extracellular matrix [142, 143], subsequently reducing wrinkle formation and laxity. Zonase enzyme from *S. salar* egg extract is available in several cosmetic products due to its effective anti-ageing mechanisms and simple recovery as a waste product from the salmon egg processing industry.

Macroalgae are also a rich and sustainable source of amino acids and peptides, of which some chlorophyte peptides have been shown to protect collagen stores and enhance collagen synthesis. A tripeptide containing an arginine–glycine–aspartic acid sequence, from the chlorophyte *Ulva lactuca*, has been reported to stimulate collagen synthesis in human fibroblasts [144]. In addition, peptides from *Chlorella vulgaris* have been shown to reduce matrix metalloproteinase-1 (MMP-1) expression in human skin cell fibroblasts [145], responsible for the breakdown of collagen. Similarly, hydrolysed *U. pertusa* has also been reported to stimulate type I collagen synthesis in human fibroblast cells via MMP-1 inhibition [146]. Chlorophytes may therefore represent a novel source of proteinaceous compounds with potential as anti-ageing effects, although it should be noted that these data are preliminary.

Astaxanthin

Other algal molecules have received attention as potential anti-ageing active ingredients. Astaxanthin (ASX), for example, belongs to a class of carotenoids present in some species of microalgae and is present in some oral supplements as an antioxidant. In addition to its antioxidant activities, it has been reported to have anti-ageing actions in both oral and topical administrations [147–153]. However, this has not been substantially investigated thus far and the majority of available literature is confined to one research group [147, 149–152]. Dietary ASX from the marine microalga *Haematococcus pluvialis* has been shown to penetrate both the dermis and epidermis in murine trials, leading to a decrease in transepidermal water loss and a visual improvement in the appearance of wrinkles, comparable to untreated controls [153]. Orally and topically administered ASX has shown significant visual improvements in the appearance of skin wrinkles, elasticity, age spots and increased cutaneous hydration in clinical trials [150]. Although the mechanism of action has not been clarified in human applications, it is suggested that the suppression of MMP-13 in mice causes the inhibition of anti-ageing features [153], where MMP-13 in mice is analogous to MMP-1 in humans [154]. Observed increases in water content of the skin suggest ASX may have applications in dry skin moisturizers as well as anti-ageing formulae.

Moisturizing molecules

Dry skin may be caused by an imbalance or reduction in the natural moisturizing factor (NMF) of the stratum corneum (SC), and a disruption to the usual process of desquamation [9, 155], and is also a symptom of ageing. The NMF is mainly comprised of amino acids, which act to maintain cutaneous hydration, thus allowing for normal desquamation and healthy skin [156, 157]. Common treatments of dry skin are topical moisturizers, which contain ingredients to mimic those comprising the NMF [158], or are formulated to encourage the occlusion or attraction of water into the epidermis.

Linoleic acid (an omega-6 fatty acid) acts as a precursor for ceramide lipid molecules, which comprise half of the extracellular lipid matrix [159], an important factor of the SC permeability barrier (SCPB). The SCPB reduces both transepidermal water loss (TEWL) and pathogenic invasion [160–162]; therefore, loss of lipid components may cause skin dryness [9, 155, 163]. Marine-derived lipids can aid in preserving skin hydration by maintaining the lipid matrix of the SC [163, 164]. Omega-3 oils, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), can be easily extracted from several marine and freshwater fish [165–167], which are naturally enriched in EPA and DHA. Barcelos *et al.* [164] administered daily omega-3 fish oils (FOs) to rats and observed the changes in dermal response to skin irritation after 30, 60 and 60 days of supplementation. After 60 days of supplementation, both irritation and TEWL were significantly reduced in response to acetone exposure. After 90 days, TEWL had reduced by 50% compared to the control group without FO. Cutaneous hydration significantly increased by 30% after 60 days of FO treatment which was maintained after 90 days, compared to controls. This supports previous claims that dietary fatty acids are transported to the SC [168, 169] and are able to improve cutaneous health through oral administration; however, this study did not assess the potential of FOs in topical moisturizers.

Similarly, the oil of the deep-sea perch, *Hoplostethus atlanticus*, has been reported to exhibit moisturizing and emollient abilities comparable to that of petroleum-based products like Vaseline® [170]. The oil produced is a wax ester composed mainly of fatty alcohols and fatty acids [171], and has been reported to improve skin dryness up to 70% as efficiently as petrolatum products [170]. However, *H. atlanticus* is reported as vulnerable to exploitation due to its late maturity, slow growth and low fecundity [172], therefore has not been considered as a sustainable source for skin moisturizing products, despite its significant moisturizing ability. This raises an important issue in recognizing the marine environment as a finite source of new cosmetic discovery, where the sustainability of target organisms should always be considered.

Similarly, the oil of squid (*Loligo loligo*) has been reported as a new source of omega-3 and omega-6 oils, where 13% of the wet weight of an adult squid equates to oil, with a high percentage of linoleic acid, EPA and DHA [173]. The culturing of squids is yet to be explored; however, *Octopus vulgaris* aquaculture is currently

being developed and has shown some early success [174]. Cephalopods are considered good candidates for successful aquaculture, due to their short life spans, early maturity and easy adaptation [175, 176]; therefore, this route of production of omega-3 and omega-6 oils merits further investigation.

Lipids act to retain water by the process of occlusion, whereas humectants such as collagen and its derivatives act differently by attracting water into the epidermis [120, 135, 177]. Collagen and collagen hydrolysate are common moisturizing active ingredients [135] with little supporting scientific evidence of their hydrating benefits. Bovine collagen sources are scrutinized due to hygiene concerns, but collagen can be derived from several marine fish [126–129], as well as organisms belonging to the Porifera [120, 178], Echinodermata [130], Cnidaria [179, 180] and Mollusca [133, 134], offering alternative sources [125], where some marine collagen has shown better biocompatibility. It should however be considered that marine collagen also has weaknesses such as a lower degradation temperature [181] and therefore more limited application than bovine sources. Jellyfish collagen is currently being used for wound dressing and scaffolding applications [182]. Recently, collagen extracted from the jellyfish *Nemopilema nomurai* has been proposed to have a significant moisturizing effect, but the data are preliminary [183]. Swatschek *et al.* [120] demonstrated the successful extraction of collagen from the marine sponge *Chondrosia reniformis*. Thirty per cent yield of freeze-dried collagen was obtained, and two cosmetic formulae were trialled on human skin. There was no significant difference in skin hydration between the sponge collagen treatments and the existing collagen product control; however, there was a significant increase in skin lipid content of 140–180 μg cm^{-2}, one hour after treatment. Despite these similarities in the efficacies of terrestrial and marine collagen as moisturizers, these preliminary data have highlighted the potential of marine collagen as an additional source of collagen.

Skin dryness is also a symptom of ageing, caused by a loss of the glycosaminoglycan (GAG) hyaluronic acid (HA), a major constituent of the dermal skin matrix found in every tissue and body fluid [183]. Hyaluronic acid is responsible for water retention, tissue regeneration and protection from ultraviolet radiation (UVR) [184–187], and its epidermal content decreases as the body ages [188], slowing moisture replenishment and tissue repair [10, 11]. This reduction also causes loss of skin elasticity, due to the decline in integral linkages between collagen and elastin that are facilitated by HA [189]. As a result, there has been an increase in moisturizers containing HA, yet only a few studies support their action of reducing wrinkles and maintaining skin moisture in topical treatment [188, 190]; therefore, there is a growing interest in discovering replacement molecules [191].

In recent years, alternative water-absorbing molecules have been investigated from marine sources. Polysaccharides, derived from the Crustacea, Phaeophyta and Rhodophyta, have been shown to possess several desirable cosmetic qualities, such as water retention, anti-inflammatory, non-toxic and broad antimicrobial action [192, 193]. Conversely, the cosmetic potential of marine bacterial exopolysaccharides (EPS) may rival that of their plant and animal counterparts due to their ease of supply, and biochemical diversity [194] – a result of the extreme environments that they inhabit. Recently, two EPS were isolated from marine bacteria, *Polaribacter* sp. SM1127 [195] and *Phyllobacterium* sp. 921F [196], which displayed significant water-absorbing properties that exceeded those shown by common cosmetic humectants, including HA. Furthermore, it has been reported that an EPS produced by *Vibrio diabolicus* stimulates the production of HA and keratinocytes, increasing the moisture content of the skin, in addition to inhibiting neuronal exocytosis, a process which promotes wrinkle formation and deepening [197]. Few examples of marine bacterial EPS have found their way into products, including Hyadisine® and Hyanify™, which are reported to stimulate the production of HA, giving rise to anti-ageing and moisturizing effects [198, 199], but their underlying mechanisms are not widely reported. With few examples of commercialized bacterial EPS, the scope for discovery of novel extremophile EPS is great, due to their relatively unexplored biochemical diversity. This may offer a promising route to new bioactive molecules with moisturizing or anti-ageing actions.

Conclusions

With the cosmetics market forecasted to be worth USD 430 billion by 2022 [200], the need for the discovery and production of new cosmetic molecules is growing. The key active molecules are set to be skincare and antioxidant compounds. There is also growing evidence that the marine environment may serve as a rich source of these substances. A great variety of molecules from marine macroalgae, including carotenoids and polyphenolic extracts, have generated attention due to several cosmetic actions. Their antioxidant, anti-melanogenic and anti-ageing properties may find application in a variety of cosmetic and pharmaceutical products. This, coupled with easy production and maintenance of macroalgae, presents an exciting and viable source of cosmetic discovery.

Marine fish have received less attention as a source of cosmetic ingredients, but are also producing molecules showing promise for applications such as antioxidants, moisturizing and anti-ageing compounds. Several fish species have exhibited high content of essential fatty acids which have shown potential as moisturizing ingredients. In addition, high collagen extraction yields from marine fish and other marine organisms have provided a platform for the easy production and application of marine-derived collagen. Other marine products include the anti-ageing enzyme Zonase from salmon eggs and extremophile bacterial EPS compounds which have moisturizing and anti-ageing properties that rival not only current moisturizing ingredients, but also molecules produced by the skin to maintain hydration. Similarly, halophytes which inhabit extreme saline environments have recently been recognized as a source of tyrosinase inhibitors and antioxidant molecules. Organisms from extreme environments offer access to a unique chemical diversity and therefore may provide an untapped resource for new bioactive molecules with applications in cosmetics. Despite these promising discoveries, the exploitation of the marine environment should be approached with caution, where the sustainability of all potential marine resources being considered.

The variety of molecules and compounds described in this review highlight the marine environment as an underexploited resource for cosmetic innovation and discovery and the data presented are crucial in shortening the pipeline to the commercialization of new and effective cosmetic products. Accessing marine chemical diversity is therefore needed to address the large and unmet need for a pipeline of new cosmetically active molecules.

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References

1. Smolinski, M.S., Hamburg, M.A. and Lederberg, J., eds. *Microbial Threats to Health: Emergence, Detection, and Response*. National Academies Press, Washington, DC (2003).
2. Morens, D.M., Folkers, G.K. and Fauci, A.S. The challenge of emerging and re-emerging infectious diseases. *Nature* **430**, 242–249 (2004).
3. King, D.A., Peckham, C., Waage, J.K., Brownlie, J. and Woolhouse, M.E.J. Infectious diseases: Preparing for the future. *Science* **313**, 1392–1393 (2006).
4. WHO. *Antimicrobial resistance* (2016). Available at: http://www.who.int/mediacentre/factsheets/fs194/en/, accessed 6 December 2016.
5. Proksch, E., Brandner, J.M. and Jensen, J.M. The skin: an indispensable barrier. *Expl. Dermatol.* **17**, 1063–1072 (2008).
6. Elias, P.M. Lipids and the epidermal permeability barrier. *Arch. Dermatol. Res.* **20**, 95–117 (1982).
7. Elias, P.M. Epidermal lipids, barrier function, and desquamation. *J. Invest. Dermatol.* **80**, 44–49 (1983).
8. Rawlings, A. and Harding, C. Moisturisation and skin barrier function. *Dermatol. Ther.* **17**, 43–48 (2004).
9. Rawlings, A., Harding, C., Watkinson, A., Banks, J., Ackerman, C. and Sabin, R. The effect of glycerol and humidity on desmosome degradation in stratum corneum. *Arch. Dermatol. Res.* **287**, 457–464 (1995).
10. Stern, R. and Jedrzejas, M.J. Hyaluronidases: their genomics, structures, and mechanisms of action. *Chem. Rev.* **106**, 818–839 (2006).
11. Jegasothy, S.M., Zabolotniaia, V. and Bielfeldt, S. Efficacy of a new topical nano-hyaluronic acid in humans. *J. Clin. Aesthet. Dermatol.* **7**, 27–29 (2014).
12. Martins, A., Vieira, H., Gaspar, H. and Santos, S. Marketed marine natural products in the pharmaceutical and cosmeceutical industries: tips for success. *Mar. Drugs* **12**, 1066–1101 (2014).
13. Kumar, S. Exploratory analysis of global cosmetic industry: major players, technology and market trends. *Technovation* **25**, 1263–1272 (2005).
14. Patel, N., Padhtare, D. and Saudagar, R.B. Newer trends in cosmetology. *World J. Pharm. Pharm. Sci.* **4**, 483–502 (2015).
15. Goossens, A. Cosmetic contact allergens. *Cosmetics* **3**, 5 (2016). https://doi.org/10.3390/cosmetics3010005.
16. Margulis, L. and Schwartz, K.V., eds. *Five Kingdoms – an Illustrated Guide to the Phyla of Life on Earth*. WH Freeman & Company, New York (1998).
17. Motuhi, S.E., Mehiri, M., Payri, C.E., La Barre, S. and Bach, S. Marine natural products from New Caledonia – a review. *Mar. Drugs* **14**, 58–118 (2016).
18. Balboa, E.M., Conde, E., Soto, M.L., Pérez-Armada, L. and Domínguez, H. Cosmetics from marine sources. In: *Springer Handbook of Marine Biotechnology* (Kim, S.-K., ed.), pp. 1015–1042. Springer, Berlin, Heidelberg (2015).
19. Parrish, J.A., Jaenicke, K.F. and Anderson, R.R. Erythema and melanogenesis action spectrum of normal human skin. *Photochem. Photobiol.* **36**, 187–191 (1982).
20. Brash, D.E., Rudolph, J.A., Simon, J.A. *et al.* A role for sunlight in skin cancer: UV-induced p53 mutations in squamous cell carcinoma. *Proc. Natl Acad. Sci. USA* **88**, 10124–10128 (1991).
21. Fisher, M.S. and Kripke, M.L. Systemic alteration induced in mice by ultraviolet irradiation and its relationship to ultraviolet carcinogenesis. *Proc. Natl Acad. Sci. USA* **74**, 1688–1692 (1997).
22. Hou, H., Li, B., Zhang, Z. *et al.* Moisture absorption and retention properties, and activity in alleviating skin photodamage of collagen polypeptide from marine fish skin. *Food Chem.* **135**, 1432–1439 (2012).
23. Cefali, L.C., Ataide, J.A., Moriel, P., Foglio, M.A. and Mazzola, P.G. Plant-based active photoprotectants for sunscreens. *Int. J. Cosmet. Sci.* **38**, 346–353 (2016).
24. Kielbassa, C., Roza, L. and Epe, B. Wavelength dependence of oxidative DNA damage induced by UV and visible light. *Carcinogenesis* **18**, 811–816 (1997).
25. Cadet, J., Douki, T. and Ravanat, J.L. Oxidatively generated damage to cellular DNA by UVB and UVA radiation. *Photochem. Photobiol.* **91**, 140–155 (2015).
26. Pfeifer, G.P. and Besaratinia, A. UV wavelength-dependent DNA damage and human non-melanoma and melanoma skin cancer. *Photochem. Photobiol. Sci.* **11**, 90–97 (2012).
27. Schwarz, T. and Schwarz, A. Molecular mechanisms of ultraviolet radiation-induced immunosuppression. *Eur. J. Cell Biol.* **90**, 560–564 (2011).
28. Barja, G. Rate of generation of oxidative stress-related damage and animal longevity. *Free Radic. Biol. Med.* **33**, 1167–1172 (2002).
29. Desbruyeres, D. and Laubier, L. *Alvinella pompejana* gen. sp. nov., aberrant Ampharetidae from East Pacific Rise hydrothermal vents. *Oceanol. Acta* **3**, 267–274 (1980).
30. Thibodeau, A. and Takeoka, A. The applications and functions of new exopolysaccharide "Deepsane" from the deepest oceans. *Fragr. J.* **34**, 61–68 (2006).
31. Lelchat, F., Cozien, J., Le Costaouec, T. *et al.* Exopolysaccharide biosynthesis and biodegradation by a marine hydrothermal *Alteromonas* sp. strain. *Appl. Microbiol. Biotechnol.* **99**, 2637–2647 (2015).
32. Le Costaouëc, T., Cérantola, S., Ropartz, D., Sinquin, C., Colliec-Jouault, S. and Boisset, C. Structural data on a bacterial exopolysaccharide produced by a deep-sea *Alteromonas macleodii* strain. *Carbohydr. Polym.* **90**, 49–59 (2012).
33. Suh, H.J., Lee, H.W. and Jung, J. Mycosporine glycine protects biological systems against photodynamic damage by quenching singlet oxygen with a high efficiency. *Photochem. Photobiol.* **78**, 109–113 (2003).
34. Dunlap, W.C. and Yamamoto, Y. Small-molecule antioxidants in marine organisms: antioxidant activity of mycosporine-glycine. *Comp. Biochem. Physiol. B* **112**, 105–114 (1995).
35. Dunlap, W.C. and Shick, J.M. Ultraviolet radiation-absorbing mycosporine-like amino acids in coral reef organisms: a biochemical and environmental perspective. *J. Phycol.* **34**, 418–430 (1998).
36. Ishihara, K., Watanabe, R., Uchida, H. *et al.* Novel glycosylated mycosporine-like amino acid, 13-O-(β-galactosyl)-porphyra-334, from the edible cyanobacterium *Nostoc sphaericum* – protective activity on human keratinocytes from UV light. *J. Photochem. Photobiol. B* **172**, 102–108 (2017).
37. Shimidzu, N., Goto, M. and Miki, W. Carotenoids as singlet oxygen quenchers in marine organisms. *Fisheries Sci.* **62**, 134–137 (1996).
38. Sachindra, N.M., Sato, E., Maeda, H., Hosokawa, M., Niwano, Y., Kohno, M. and Miyashita, K. Radical scavenging and singlet oxygen quenching activity of marine carotenoid fucoxanthin and its metabolites. *J. Agric. Food Chem.* **55**, 8516–8522 (2007).
39. Rodrigues, E., Mariutti, L.R. and Mercadante, A.Z. Scavenging capacity of marine carotenoids against reactive oxygen and nitrogen species in a membrane-mimicking system. *Mar. Drugs* **10**, 1784–1798 (2012).
40. Bar-Or, D., Bar-Or, R., Rael, L.T. and Brody, E.N. Oxidative stress in severe acute illness. *Redox. Biol.* **4**, 340–345 (2015).

41. Pietta, P., Minoggio, M. and Bramati, L. Plant polyphenols: structure, occurrence and bioactivity. *Stud. Nat. Prod. Chem.* **28**, 257–312 (2003).
42. Heo, S.-J., Ko, S.-C., Kang, S.-M. *et al.* Inhibitory effect of diphlorethohydroxycarmalol on melanogenesis and its protective effect against UV-B radiation-induced cell damage. *Food Chem. Toxicol.* **48**, 1355–1361 (2010).
43. Cha, S.-H., Ko, C.-I., Kim, D. and Jeon, Y.-J. Protective effects of phlorotannins against ultraviolet B radiation in zebrafish (*Danio rerio*). *Vet. Dermatol.* **23**, 51–57 (2012).
44. Le Lann, K., Surget, G., Couteau, C. *et al.* Sunscreen, antioxidant, and bactericide capacities of phlorotannins from the brown macroalga *Halidrys siliquosa*. *J. Appl. Phycol.* **28**, 3547–3559 (2016).
45. Ko, S.-C., Cha, S.-H., Heo, S.-J., Lee, S.-H., Kang, S.-M. and Jeon, Y.-J. Protective effect of *Ecklonia cava* on UVB-induced oxidative stress: in vitro and in vivo zebrafish model. *J. Appl. Phycol.* **23**, 697–708 (2011).
46. Kim, K.C., Piao, M.J., Zeng, J. *et al.* Fucodiphlorethol G purified from *Ecklonia cava* suppresses ultraviolet B radiation-induced oxidative stress and cellular damage. *Biomol. Ther.* **22**, 301–307 (2014).
47. Sinha, R.P., Singh, S.P. and Häder, D.P. Database on mycosporines and mycosporine-like amino acids (MAAs) in fungi, cyanobacteria, macroalgae, phytoplankton and animals. *J. Photochem. Photobiol. B* **89**, 29–35 (2007).
48. Jain, S., Prajapat, G., Abrar, M., Ledwani, L., Singh, A. and Agrawal, A. Cyanobacteria as efficient producers of mycosporine-like amino acids. *J. Basic Microbiol.* (2017). https://doi.org/10.1002/jobm.201700044.
49. Carreto, J.I. and Carignan, M.O. Mycosporine-like amino acids: relevant secondary metabolites. Chemical and Ecological Aspects. *Mar. Drugs* **9**, 387–446 (2011).
50. Dunlap, W.C., Chalker, B.E. and Oliver, J.K. Bathymetric adaptations of reef-building corals at Davies Reef, Australia. III. UV-B absorbing compounds. *J. Exp. Mar. Biol. Ecol.* **104**, 239–248 (1986).
51. Lee, J.H., Kim, H.S., Seo, H.H. *et al.* Antiaging effects of algae-derived mycosporine-like amino acids (MAAs) on skin. In: *Textbook of Aging Skin* (Farage, M.A., Miller, K.W. and Maibach, H.I., eds.), pp. 1–8. Springer-Verlag, Berlin (2015).
52. Karentz, D., McEuen, F.S., Land, M.C. and Dunlap, W.C. Survey of mycosporine-like amino acid compounds in Antarctic marine organisms: potential protection from ultraviolet exposure. *Mar. Biol.* **108**, 157–166 (1991).
53. Karentz, D. and Lutze, L.H. Evaluation of biologically harmful ultraviolet radiation in Antarctica with a biological dosimeter designed for aquatic environments. *Limnol. Oceanogr.* **35**, 549–556 (1990).
54. Bernhard, G., Dahlback, A., Fioletov, V. *et al.* High levels of ultraviolet radiation observed by ground-based instruments below the 2011 Arctic ozone hole. *Atmos. Chem. Phys.* **13**, 10573–10590 (2013).
55. Garcia-Corral, L.S., Holding, J.M., Carrillo-de-Albornoz, P. *et al.* Effects of UVB radiation on net community production in the upper global ocean. *Global Ecol. Biogeogr.* **1**, 54–64 (2016).
56. Karsten, U. and Wiencke, C. Factors controlling the formation of UV-absorbing mycosporine-like amino acids in the marine red alga *Palmaria palmata* from Spitsbergen (Norway). *J. Plant Physiol.* **155**, 407–415 (1999).
57. De la Coba, F., Aguilera, J., Figueroa, F.L., De Gálvez, M.V. and Herrera, E. Antioxidant activity of mycosporine-like amino acids isolated from three red macroalgae and one marine lichen. *J. Appl. Phycol.* **21**, 161–169 (2009).
58. Figueroa, L.F., Álvarez, F., Celis-Plá, P. *et al.* The accumulation of UV screen photoprotectors (mycosporine-like amino acids) in red macroalgae is influenced by nitrogen availability. Unpublished thesis. Málaga, University of Málaga (2015).
59. Torres, P.B., Chow, F., Ferreira, M.J. and dos Santos, D.Y. Mycosporine-like amino acids from *Gracilariopsis tenuifrons* (Gracilariales, Rhodophyta) and its variation under high light. *J. Appl. Phycol.* **28**, 2035–2040 (2016).
60. Buege, J.A. and Aust, S.D. Microsomal lipid peroxidation. *Method. Enzymol.* **52**, 302–310 (1978).
61. (Halliwell, B. and Gutteridge, J.M., eds.) *Free Radicals in Biology and Medicine*. Oxford University Press, New York (2015).
62. Cardozo, K.H.M., Guaratini, T., Barros, M.P. *et al.* Metabolites from algae with economical impact. *Comp. Biochem. Physiol. C Toxicol. Pharmacol.* **146**, 60–78 (2007).
63. Colabella, F., Moliné, M. and Libkind, D. UV sunscreens of microbial origin: mycosporines and mycosporine-like amino acids. *Recent Pat. Biotechnol.* **8**, 179–193 (2015).
64. De la Coba, F., Aguilera, J., De Galvez, M.V., Alvarez, M., Gallego, E., Figueroa, F.L. and Herrera, E. Prevention of the ultraviolet effects on clinical and histopathological changes, as well as the heat shock protein-70 expression in mouse skin by topical application of algal UV-absorbing compounds. *J. Dermatol. Sci.* **55**, 161–169 (2009).
65. Fionda, C., Abruzzese, M.P., Santoni, A. and Cippitelli, M. Immunoregulatory and effector activities of nitric oxide and reactive nitrogen species in cancer. *Curr. Med. Chem.* **23**, 2618–2636 (2016).
66. Chuyen, H.V. and Eun, J.B. Marine carotenoids: bioactivities and potential benefits to human health. *Crit. Rev. Food Sci.* **57**, 2600–2610 (2017).
67. Zhang, H. and Tsao, R. Dietary polyphenols, oxidative stress and antioxidant and anti-inflammatory effects. *Curr. Opin. Food Sci.* **8**, 33–42 (2016).
68. Waller, U., Buhmann, A.K., Ernst, A. *et al.* Integrated multi-trophic aquaculture in a zero-exchange recirculation aquaculture system for marine fish and hydroponic halophyte production. *Aquacult. Int.* **23**, 1473–1489 (2015).
69. Lopes, A., Rodrigues, M.J., Pereira, C. *et al.* Natural products from extreme marine environments: searching for potential industrial uses within extremophile plants. *Ind. Crops Prod.* **94**, 299–307 (2016).
70. Aboul-Enein, A.M., El Baz, F.K., El-Baroty, G.S., Youssef, A.M. and El-Baky, Abd H.H. Antioxidant activity of algal extracts on lipid peroxidation. *J. Med. Sci.* **3**, 87–98 (2003).
71. Adjimani, J.P. and Asare, P. Antioxidant and free radical scavenging activity of iron chelators. *Toxicol. Rep.* **2**, 721–728 (2015).
72. Jack, A.R., Norris, P.L. and Storrs, F.J. Allergic contact dermatitis to plant extracts in cosmetics. *Semin. Cutan. Med. Surg.* **32**, 140–146 (2013).
73. Corazza, M., Borghi, A., Gallo, R. *et al.* Topical botanically derived products: use, skin reactions, and usefulness of patch tests. A multicenter Italian study. *Contact Dermatit.* **70**, 90–97 (2014).
74. Singh, I.P. and Bharate, S.B. Phloroglucinol compounds of natural origin. *Nat. Prod. Rep.* **23**, 558–591 (2006).
75. Hamed, I., Ozogul, F., Ozogul, Y. and Regenstein, J.M. Marine bioactive compounds and their health benefits: a review. *Compr. Rev. Food Sci. Food Saf.* **14**, 446–465 (2015).
76. Heffernan, N., Brunton, N.P., FitzGerald, R.J. and Smyth, T.J. Profiling of the molecular weight and structural isomer abundance of macroalgae-derived phlorotannins. *Mar. Drugs* **13**, 509–528 (2015).
77. Cao, G., Sofic, E. and Prior, R.L. Antioxidant and prooxidant behaviour of

flavonoids: structure-activity relationships. *Free Radic. Biol. Med.* **22**, 749–760 (1997).
78. Pannala, S., Chan, T.S., O'Brien, P.J. and Rice-Evans, C.A. Flavonoids B-ring chemistry and antioxidant activity: fast reaction kinetics. *Biochem. Biophys. Res. Commun.* **282**, 1161–1168 (2001).
79. Huovinen, P. and Gómez, I. UV sensitivity of vegetative and reproductive tissues of two Antarctic brown algae is related to differential allocation of phenolic substances. *Photochem. Photobiol.* **91**, 1382–1388 (2015).
80. Heo, S.-J., Ko, S.-C., Cha, S.-H. *et al.* Effect of phlorotannins isolated from *Ecklonia cava* on melanogenesis and their protective effect against photo-oxidative stress induced by UV-B radiation. *Toxicol. In Vitro* **23**, 1123–1130 (2009).
81. Correia-da-Silva, M., Sousa, E. and Pinto, M.M. Emerging sulfated flavonoids and other polyphenols as drugs: nature as an inspiration. *Med. Res. Rev.* **34**, 223–279 (2014).
82. Zillich, O.V., Schweiggert-Weisz, U., Eisner, P. and Kerscher, M. Polyphenols as active ingredients for cosmetic products. *Int. J. Cosmet. Sci.* **37**, 455–464 (2015).
83. Gilchrest, B.A. and Szabo, G. Effects of aging and chronic sun exposure on melanocytes in human skin. *J. Invest. Dermatol.* **73**, 141–143 (1979).
84. Coelho, S.G., Valencia, J.C., Yin, L. *et al.* UV exposure modulates hemidesmosome plasticity, contributing to long-term pigmentation in human skin. *J. Pathol.* **236**, 17–29 (2015).
85. Hearing, V.J. and Jimenez, M. Mammalian tyrosinase-the critical regulatory control point in melanocyte pigmentation. *Int. J. Biochem.* **19**, 1141–1147 (1987).
86. Chen, C.Y., Lin, L.C., Yang, W.F., Bordon, J. and Wang, H.M.D. An updated organic classification of tyrosinase inhibitors on melanin biosynthesis. *Curr. Org. Chem.* **19**, 4–18 (2015).
87. Nag, T.C. Ultrastructural changes in the melanocytes of aging human choroid. *Micron* **79**, 16–23 (2015).
88. Song, T.Y., Chen, C.H., Yang, N.C. and Fu, C.S. The correlation of *in vitro* mushroom tyrosinase activity with cellular tyrosinase activity and melanin formation in melanoma cells A2058. *J. Food Drug Anal.* **17**, 156–162 (2009).
89. Lee, A.Y. and Noh, M. The regulation of epidermal melanogenesis via cAMP and/or PKC signaling pathways: insights for the development of hypopigmenting agents. *Arch. Pharm. Res.* **36**, 792–801 (2013).
90. Haddad, A.L., Matos, L.F., Brunstein, F., Ferreira, L.M., Silva, A. and Costa, D. A clinical, prospective, randomized, double-blind trial comparing skin whitening complex with hydroquinone vs. placebo in the treatment of melasma. *Int. J. Dermatol.* **42**, 153–156 (2003).
91. Gupta, A.K., Gover, M.D., Nouri, K. and Taylor, S. The treatment of melasma: a review of clinical trials. *J. Am. Acad. Dermatol.* **55**, 1048–1065 (2006).
92. Momtaz, S., Mapunya, B.M., Houghton, P.J., Edgerly, C., Hussein, A., Naidoo, S. and Lall, N. Tyrosinase inhibition by extracts and constituents of *Sideroxylon inerme L.* stem bark, used in South Africa for skin lightening. *J. Ethnopharmacol.* **119**, 507–512 (2008).
93. Nakagawa, M., Kawai, K. and Kawai, K. Contact allergy to kojic acid in skin care products. *Contact Dermatit.* **32**, 9–13 (1995).
94. García-Gavín, J., González-Vilas, D., Fernández-Redondo, V. and Toribio, J. Pigmented contact dermatitis due to kojic acid. A paradoxical side effect of a skin lightener. *Contact Dermatit.* **62**, 63–64 (2010).
95. Khotimchenko, Y.S. Tyrosinase inhibitors from marine algae. *Br. J. Dermatol.* **175**, 457–458 (2016).
96. Yuan, J.-P., Peng, J., Yin, K. and Wang, J.-H. Potential health-promoting effects of astaxanthin: a high-value carotenoid mostly from microalgae. *Mol. Nutr. Food Res.* **55**, 150–165 (2011).
97. Chan, Y.Y., Kim, K.H. and Cheah, S.H. Inhibitory effects of *Sargassum polycystum* on tyrosinase activity and melanin formation in B16F10 murine melanoma cells. *J. Ethnopharmacol.* **137**, 1183–1188 (2011).
98. Kang, H.S., Kim, H.R., Byun, D.S., Son, B.W., Nam, T.J. and Choi, J.S. Tyrosinase inhibitors isolated from the edible brown alga *Ecklonia stolonifera*. *Arch. Pharm. Res.* **27**, 1226–1232 (2004).
99. Cha, S.H., Ko, S.C., Kim, D. and Jeon, Y.J. Screening of marine algae for potential tyrosinase inhibitor: those inhibitors reduced tyrosinase activity and melanin synthesis in zebrafish. *J. Dermatol.* **38**, 354–363 (2011).
100. Działo, M., Mierziak, J., Korzun, U., Preisner, M., Szopa, J. and Kulma, A. The potential of plant phenolics in prevention and therapy of skin disorders. *Int. J. Mol. Sci.* **17**, 160–201 (2016).
101. Kwak, J.Y., Seok, J.K., Suh, H.J., Choi, Y.H., Hong, S.S., Kim, D.S. and Boo, Y.C. Anti-melanogenic effects of luteolin 7-sulfate isolated from Phyllospadix iwatensis Makino. *Br. J. Dermatol.* **175**, 501–511 (2016).
102. Shimizu, K., Kondo, R. and Sakai, K. Inhibition of tyrosinase by flavonoids, stilbenes and related 4-substituted resorcinols: structure-activity investigations. *Planta Med.* **66**, 11–15 (2000).
103. Song, Y.S., Balcos, M.C., Yun, H.Y., Baek, K.J., Kwon, N.S., Kim, M.K. and Kim, D.S. Erk activation by fucoidan leads to inhibition of melanogenesis in mel-ab cells. *Korean J. Physiol. Pharmacol.* **19**, 29–34 (2015).
104. Wang, Z.J., Wei, X., Liang, J.W., Wang, C.S. and Kang, Y. Effect of fucoidan on B16 murine melanoma cell melanin formation and apoptosis. *Afr. J. Tradit. Complement. Altern. Med.* **14**, 149–155 (2017).
105. Kim, D.S., Park, S.H., Kwon, S.B., Park, E.S., Huh, C.H., Youn, S.W. and Park, K.C. Sphingosylphosphorylcholine-induced ERK activation inhibits melanin synthesis in human melanocytes. *Pigm. Cell Res.* **19**, 146–153 (2006).
106. Kondo, T. and Hearing, V.J. Update on the regulation of mammalian melanocyte function and skin pigmentation. *Expert Rev. Dermatol.* **6**, 97–108 (2011).
107. Dooley, T.P., Gadwood, R.C., Kilgore, K. and Thomasco, L.M. Development of an in vitro primary screen for skin depigmentation and antimelanoma agents. *Skin Pharmacol. Physiol.* **7**, 188–200 (1994).
108. Matthews, I. *Trends in facial skin care* (2013). Available at: http://www.specialchem4cosmetics.com/services/articles.aspx?id_10598&lr_tfcos1401251&li_30020670, accessed 7 March 2014.
109. Chonody, J.M. and Teater, B. Why do I dread looking old?: a test of social identity theory, terror management theory, and the double standard of aging. *J. Women Aging* **28**, 112–126 (2016).
110. Helfrich, Y.R., Sachs, D.L. and Voorhees, J.J. Overview of skin aging and photoaging. *Dermatol. Nurs.* **20**, 177–183 (2008).
111. Matsubara, A. Differences in the surface and subsurface reflection characteristics of facial skin by age group. *Skin Res. Tech.* **18**, 29–35 (2012).
112. Wang-Michelitsch, J. and Michelitsch, T.M. Tissue fibrosis: a principle evidence for the central role of misrepairs in aging. *arXiv preprint arXiv:1505.01376* (2015).
113. Helenius, M., Makelainen, L. and Salminen, A. Attenuation of NF-kB signalling response to UVB light during cellular senescence. *Exp. Cell Res.* **248**, 194–202 (1999).
114. Seite, S., Colige, A., Deroanne, C. *et al.* Changes in matrix gene and protein

expressions after single or repeated exposure to one minimal erythemal dose of solar-simulated radiation in human skin *in vivo*. *Photochem. Photobiol.* **79**, 265–271 (2004).
115. Wang, J., Michelitsch, T., Wunderlin, A. and Mahadeva, R. Aging as a consequence of misrepair – a novel theory of aging. *arXiv preprint arXiv:0904.0575* (2009).
116. Varani, J., Dame, M.K., Rittie, L., Fligiel, S.E., Kang, S., Fisher, G.J. and Voorhees, J.J. Decreased collagen production in chronologically aged skin: roles of age-dependent alteration in fibroblast function and defective mechanical stimulation. *Am. J. Pathol.* **168**, 1861–1868 (2006).
117. Li, G.Y., Fukunaga, S., Takenouchi, K. and Nakamura, F. Comparative study of the physiological properties of collagen, gelatin and collagen hydrolysate as cosmetic materials. *Int. J. Cosmet. Sci.* **27**, 101–106 (2005).
118. Shigemura, Y., Iwai, K., Morimatsu, F. *et al.* Effect of prolyl-hydroxyproline (Pro-Hyp), a food-derived collagen peptide in human blood, on growth of fibroblasts from mouse skin. *J. Agric. Food Chem.* **57**, 444–449 (2009).
119. Tanaka, M., Koyama, Y.I. and Nomura, Y. Effects of collagen peptide ingestion on UV-B-induced skin damage. *Biosci. Biotech. Bioch.* **73**, 930–932 (2009).
120. Matsuda, N., Koyama, Y.I., Hosaka, Y. *et al.* Effects of ingestion of collagen peptide on collagen fibrils and glycosaminoglycans in the dermis. *J. Nutr. Sci. Vitaminol.* **52**, 211–215 (2006).
121. Swatschek, D., Schatton, W., Kellermann, J., Müller, W.E. and Kreuter, J. Marine sponge collagen: isolation, characterization and effects on the skin parameters surface-pH, moisture and sebum. *Eur. J. Pharm. Biopharm.* **53**, 107–113 (2002).
122. Giraud-Guille, M.-M., Besseau, L., Chopin, C., Durand, P. and Herbage, D. Structural aspects of fish skin collagen which forms ordered arrays via liquid crystalline states. *Biomaterials* **21**, 899–906 (2000).
123. Li, H., Liu, B.L., Gao, L.Z. and Chen, H.L. Studies on bullfrog skin collagen. *Food Chem.* **84**, 65–69 (2004).
124. Ogawa, M., Portier, R.J., Moody, M.W., Bell, J., Schexnayder, M.A. and Losso, J.N. Biochemical properties of bone and scale collagens isolated from the subtropical fish black drum (*Pogonia cromis*) and sheepshead seabream (*Archosargus probatocephalus*). *Food Chem.* **88**, 495–501 (2004).
125. Subhan, F., Ikram, M., Shehzad, A. and Ghafoor, A. Marine collagen: an emerging player in biomedical applications. *J. Food Sci. Tech.* **52**, 4703–4707 (2015).
126. Song, E., Kim, S.Y., Chun, T., Byun, H.J. and Lee, Y.M. Collagen scaffolds derived from a marine source and their biocompatibility. *Biomaterials* **27**, 2951–2961 (2006).
127. Devictor, P., Allard, R., Perrier, E. and Huc, A. Unpigmented fish skin, particularly from flat fish, as a novel industrial source of collagen, extraction method, collagen and biomaterial thereby obtained. US Patent 5420248. Coletica, Lyon (1995).
128. Nagai, T. and Suzuki, N. Isolation of collagen from fish waste material – skin, bone and fins. *Food Chem.* **68**, 277–281 (2000a).
129. Nagai, T. and Suzuki, N. Preparation and characterization of several fish bone collagens. *J. Food Biochem.* **24**, 427–436 (2000c).
130. Nagai, T., Araki, Y. and Suzuki, N. Collagen of the skin of ocellate puffer fish (*Takifugu rubripes*). *Food Chem.* **78**, 173–177 (2002).
131. Nagai, T. and Suzuki, N. Partial characterization of collagen from purple sea urchin (*Anthocidaris crassispina*) test. *Int. J. Food Sci. Tech.* **35**, 497–501 (2000b).
132. Nagai, T., Ogawa, T., Nakamura, T. *et al.* Collagen of edible jellyfish exumbrella. *J. Sci. Food Agric.* **79**, 855–858 (1999).
133. Nagai, T., Worawattanamateekul, W., Suzuki, N. *et al.* Isolation and characterization of collagen from rhizostomous jellyfish (*Rhopilema asamushi*). *Food Chem.* **70**, 205–208 (2000).
134. Nagai, T., Yamashita, E., Taniguchi, K., Kanamori, N. and Suzuki, N. Isolation and characterisation of collagen from the outer skin waste material of cuttlefish (*Sepia lycidas*). *Food Chem.* **72**, 425–429 (2001).
135. Nagai, T. and Suzuki, N. Preparation and partial characterization of collagen from paper nautilus (*Argonauta argo*, Linnaeus) outer skin. *Food Chem.* **76**, 149–153 (2002).
136. Langmaier, F., Mladek, M., Kolomaznik, K. and Sukop, S. Collagenous hydrolysates from untraditional sources of proteins. *Int. J. Cosmet. Sci.* **23**, 193–199 (2001).
137. Thring, T.S., Hili, P. and Naughton, D.P. Anti-collagenase, anti-elastase and anti-oxidant activities of extracts from 21 plants. *BMC Complement Altern. Med.* **9**, 27 (2009). https://doi.org/10.1186/1472-6882-9-27.
138. Karim, A.A., Azlan, A., Ismail, A., Hashim, P., Gani, S.S.A., Zainudin, B.H. and Abdullah, N.A. Phenolic composition, antioxidant, anti-wrinkles and tyrosinase inhibitory activities of cocoa pod extract. *BMC Complement Altern. Med.* **14**, 381–395 (2014).
139. Fitton, J.H., Dell'Acqua, G., Gardiner, V.A., Karpiniec, S.S., Stringer, D.N. and Davis, E. Topical benefits of two fucoidan-rich extracts from marine macroalgae. *Cosmetics* **2**, 66–81 (2015).
140. Gräff, J., Kahn, M., Samiei, A., Gao, J., Ota, K.T., Rei, D. and Tsai, L.H. A dietary regimen of caloric restriction or pharmacological activation of SIRT1 to delay the onset of neurodegeneration. *J. Neurosci.* **33**, 8951–8960 (2013).
141. Lønne, G.K., Gammelsæter, R. and Haglerød, C. Composition characterization and clinical efficacy study of a salmon egg extract. *Int. J. Cosmet. Sci.* **35**, 515–522 (2013).
142. Mukherjee, S., Date, A., Patravale, V., Korting, H.C., Roeder, A. and Weindl, G. Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety. *Clin. Interv. Aging* **1**, 327–348 (2006).
143. Mahoney, M.G., Brennan, D., Starcher, B., Faryniarz, J., Ramirez, J., Parr, L. and Uitto, J. Extracellular matrix in cutaneous aging: the effects of 0.1% copper–zinc malonate-containing cream on elastin biosynthesis. *Exp. Dermatol.* **18**, 205–211 (2009).
144. Guglielmo, M. and Montanari, D. Cosmetic composition with a lifting effect for sustaining relaxed tissues. WO Patent 2008146116. Labo Cosprophar AG, Basel (2008).
145. Chen, C.L., Liou, S.F., Chen, S.J. and Shih, M.F. Protective effects of Chlorella-derived peptide on UVB-induced production of MMP-1 and degradation of procollagen genes in human skin fibroblasts. *Regul. Toxicol. Pharm.* **60**, 112–119 (2011).
146. Ko, H.J., Kim, G.B., Lee, D.H., Lee, G.S. and Pyo, H.B. The effect of hydrolyzed Jeju *Ulva pertusa* on the proliferation and type I collagen synthesis in replicative senescent fibroblasts. *J. Soc. Cosmet. Sci. Korea* **39**, 177–186 (2013).
147. Yamashita, E. Suppression of post-UVB hyperpigmentation by topical astaxanthin from krill. *Fragr. J.* **14**, 180–185 (1995).
148. Arakane, K. Superior skin protection via astaxanthin. *Carotenoid Sci.* **5**, 21–24 (2002).
149. Yamashita, E. The effects of a dietary supplement containing astaxanthin on skin condition. *Carotenoid Sci.* **10**, 91–95 (2006).
150. Tominaga, K., Hongo, N., Karato, M. and Yamashita, E. Cosmetic benefits of astaxanthin on human subjects. *Acta Biochim. Pol.* **59**, 43–47 (2012).
151. Seki, T., Sueki, H., Kono, H., Suganuma, K. and Yamashita, E. Effects of astaxanthin

from *Haematococcus pluvialis* on human skin-patch test; skin repeated application test; effect on wrinkle reduction. *Fragr. J.* **12**, 98–103 (2001).
152. Yamashita, E. Cosmetic benefit of dietary supplements including astaxanthin and tocotrienol on human skin. *Food Style* **21**, 112–117 (2002).
153. Komatsu, T., Sasaki, S., Manabe, Y., Hirata, T. and Sugawara, T. Preventive effect of dietary astaxanthin on UVA-induced skin photoaging in hairless mice. *PLoS ONE* **12**, e0171178 (2017).
154. Mariani, T.J., Sandefur, S., Roby, J.D. and Pierce, R.A. Collagenase-3 induction in rat lung fibroblasts requires the combined effects of tumor necrosis factor-alpha and 12-lipoxygenase metabolites: a model of macrophage-induced, fibroblast-driven extracellular matrix remodeling during inflammatory lung injury. *Mol. Biol. Cell* **9**, 1411–1424 (1998).
155. Rawlings, A.V. and Voegeli, R. Stratum corneum proteases and dry skin conditions. *Cell Tissue Res.* **351**, 217–235 (2013).
156. Harding, C.R., Watkinson, A., Rawlings, A.V. and Scott, I.R. Dry skin, moisturisation and corneodesmolysis. *Int. J. Cosmet. Sci.* **22**, 21–52 (2000).
157. Feng, L., Chandar, P., Lu, N., Vincent, C., Bajor, J. and McGuiness, H. Characteristic differences in barrier and hygroscopic properties between normal and cosmetic dry skin II Depth profile of natural moisturizing factor and cohesivity. *Int. J. Cosmet. Sci.* **36**, 231–238 (2014).
158. Rawlings, A., Canestrari, D. and Dobkowski, B. Moisturizer technology versus clinical performance. *Dermatol. Ther.* **17**, 49–56 (2004).
159. Wertz, P.W. Biochemistry of human stratum corneum lipids. In: *Skin Barrier* (Elias, P.M. and Feingold, K.R., eds.), pp. 33–42. Taylor & Francis, New York (2006).
160. Elias, P.M., Brown, B.E. and Ziboh, V.A. The permeability barrier in essential fatty acid deficiency: evidence for a direct role for linoleic acid in barrier function. *J. Invest. Dermatol.* **74**, 230–233 (1980).
161. Lodén, M. Moisturizers: treatment of dry skin syndrome and barrier defects. In: *Cosmeceuticals and Active Cosmetics* (Sivamani, R.K., Jagdeo, J.R., Elsner, P. and Maibach, H.I., eds.), pp. 61–70. CRC Press, Boca Raton (2015).
162. Garidel, P., Fölting, B., Schaller, I. and Kerth, A. The microstructure of the stratum corneum lipid barrier: mid-infrared spectroscopic studies of hydrated ceramide: palmitic acid: cholesterol model systems. *Biophys. Chem.* **150**, 144–156 (2010).
163. Meguro, S., Arai, Y., Masukawa, Y., Uie, K. and Tokimitsu, I. Relationship between covalently bound ceramides and transepidermal water loss (TEWL). *Arch. Dermatol. Res.* **292**, 463–468 (2000).
164. Barcelos, R.C., de Mello-Sampayo, C., Antoniazzi, C.T. *et al.* Oral supplementation with fish oil reduces dryness and pruritus in the acetone-induced dry skin rat model. *J. Dermatol. Sci.* **79**, 298–304 (2015).
165. Gbogouri, G.A., Linder, M., Fanni, J. and Parmentier, M. Analysis of lipids extracted from salmon (*Salmo salar*) heads by commercial proteolytic enzymes. *Eur. J. Lipid Sci. Tech.* **108**, 766–775 (2006).
166. Larsson, S.C., Kumlin, M., Ingelman-Sundberg, M. and Wolk, A. Dietary long-chain n-3 fatty acids for the prevention of cancer: a review of potential mechanisms. *Am. J. Clin. Nutr.* **79**, 935–945 (2004).
167. Wang, D.H., Jackson, J.R., Twining, C. *et al.* Saturated branched chain, normal odd-carbon-numbered, and n-3 (omega-3) polyunsaturated fatty acids in freshwater fish in the northeastern United States. *J. Agric. Food Chem.* **64**, 7512–7519 (2016).
168. Menon, G.K., Feingold, K.R., Moser, A.H., Brown, B.E. and Elias, P.M. De novo sterologenesis in the skin, II. Regulation by cutaneous barrier requirements. *J. Lipid Res.* **26**, 418–427 (1985).
169. Grubauer, G., Feingold, K.R. and Elias, P.M. Relationship of epidermal lipogenesis to cutaneous barrier function. *J. Lipid Res.* **28**, 746–752 (1987).
170. Domoto, N., Koriyama, T., Chu, B.S. and Tsuji, T. Evaluation of the efficacy of orange roughy (*Hoplostethus atlanticus*) oil in subjects with dry skin. *Int. J. Cosmet. Sci.* **34**, 322–327 (2012).
171. Buisson, D.H., Body, D.R., Dougherty, G.J., Eyres, L. and Vlieg, P. Oil from deep water fish species as a substitute for sperm whale and jojoba oils. *J. Am. Oil Chem. Soc.* **59**, 390–395 (1982).
172. Minto, C. and Nolan, C.P. Fecundity and maturity of orange roughy (*Hoplostethus atlanticus* Collett 1889) on the Porcupine Bank, northeast Atlantic. *Environ. Biol. Fish.* **77**, 39–50 (2006).
173. Asadpour, Y.A. Squid (*Loligo loligo*): the new source to extract omega-3 and omega-6 rich marine oils. *Iran. J. Fish. Sci.* **15**, 100–107 (2016).
174. Iglesias, J. and Fuentes, L. *Octopus vulgaris*. Paralarval culture. In: *Cephalopod Culture* (Iglesias, J., Fuentes, L. and Villanueva, R., eds.), pp. 427–450. Springer, Dordrecht (2014).
175. Iglesias, J., Sánchez, F.J., Otero, J.J. and Moxica, C. Culture of octopus (*Octopus vulgaris*, Cuvier): present knowledge, problems and perspectives. *Cahiers Options Méditerranéennes* **47**, 313–321 (2000).
176. Navarro, J.C. and Villanueva, R. The fatty acid composition of Octopus vulgaris paralarvae reared with live and inert food: deviation from their natural fatty acid profile. *Aquaculture* **219**, 613–631 (2003).
177. Garrone, R. The collagen of the Porifera. In: *Biology of Invertebrate and Lower Invertebrate Collagens (Bairati, A* (Garrone, R., ed.), pp. 157–175. Plenum Press, London (1985).
178. Kimura, S., Miura, S. and Park, Y.S. Collagen as the major edible component of jellyfish. *J. Food Sci.* **48**, 1758–1760 (1983).
179. Miura, S. and Kimura, S. Jellyfish mesogloea collagen. *J. Biol. Chem.* **260**, 16352–16356 (1985).
180. Zhang, Z., Li, G. and Shi, B.I. Physicochemical properties of collagen, gelatin and collagen hydrolysate derived from bovine limed split wastes. *J. Soc. Leath. Tech. Ch.* **90**, 23–28 (2006).
181. Jellagen. *Next generation collagen* (2017). Available at: http://www.jellagen.co.uk, accessed 4 July 2017.
182. Kim, D.W., Baek, T.S., Kim, Y.J., Choi, S.K. and Lee, D.W. Moisturizing effect of jellyfish collagen extract. *J. Soc. Cosmet. Sci. Korea* **42**, 153–162 (2016).
183. Fraser, J.R.E., Laurent, T.C. and Laurent, U.B.G. Hyaluronan: its nature, distribution, functions and turnover. *J. Intern. Med.* **242**, 27–33 (1997).
184. Laurent, T.C. and Fraser, J.R. Hyaluronan. *FASEB J.* **6**, 2397–2404 (1992).
185. Sherman, L., Sleeman, J., Herrlich, P. and Ponta, H. Hyaluronate receptors: key players in growth, differentiation, migration and tumor progression. *Curr. Opin. Cell Biol.* **6**, 726–733 (1994).
186. Tzellos, T.G., Klagas, I., Vahtsevanos, K. *et al.* Extrinsic aging in the human skin is associated with alterations in the expression of hyaluronic acid and its metabolizing enzymes. *Exp. Dermatol.* **18**, 1028–1035 (2009).
187. Ganceviciene, R., Liakou, A.I., Theodoridis, A., Makrantonaki, E. and Zouboulis, C.C. Skin anti-aging strategies. *Dermatoendocrinol.* **4**, 308–319 (2012).
188. Goberdhan, L., Makino, E., Fleck, T. and Mehta, R. Immediate and long-term effects of a topical serum with five forms of hyaluronic acid on facial wrinkles and intrinsic skin moisture content. *J. Am. Acad. Dermatol.* **74**, AB18 (2016). https://doi.org/10.1016/j.jaad.2016.02.072.
189. Ghersetich, I., Lotti, T., Campanile, G., Grappone, C. and Dini, G. Hyaluronic acid

in cutaneous intrinsic aging. *Int. J. Dermatol.* **33**, 119–122 (1994).
190. Pavicic, T., Gauglitz, G.G., Lersch, P., Schwach-Abdellaoui, K., Malle, B., Korting, H.C. and Farwick, M. Efficacy of cream based formulations of hyaluronic acid of different molecular weights in anti-wrinkle treatment. *J. Drugs Dermatol.* **10**, 990–1000 (2011).
191. Baumann, L. Skin aging and its treatment. *J. Pathol.* **211**, 241–251 (2007).
192. Yanase, Y., Hiragun, T., Uchida, K. *et al.* Peritoneal injection of fucoidan suppresses the increase of plasma IgE induced by OVA-sensitization. *Biochem. Bioph. Res. Commun.* **387**, 435–439 (2009).
193. Singh, R., Chacharkar, M.P. and Mathur, A.K. Chitin membrane for wound dressing application – preparation, characterisation and toxicological evaluation. *Int. Wound J.* **5**, 665–673 (2008).
194. MacCormick, C.A., Harris, J.E., Jay, A.J., Ridout, M.J., Colquhoun, I.J. and Morris, V.J. Isolation and characterization of new extracellular polysaccharide from an *Acetobacter* species. *J. Appl. Bacteriol.* **81**, 419–424 (1996).
195. Sun, M.L., Zhao, F., Shi, M., Zhang, X.Y., Zhou, B.C., Zhang, Y.Z. and Chen, X.L. Characterization and biotechnological potential analysis of a new exopolysaccharide from the Arctic marine bacterium *Polaribacter* sp. SM1127. *Nat. Sci. Rep.* **5**, 18435 (2015). https://doi.org/10.1038/srep18435.
196. Li, Y., Zhang, G., Du, C. *et al.* Characterization of high yield exopolysaccharide produced by *Phyllobacterium* sp. 921F exhibiting moisture preserving properties. *Int. J. Biol. Macromol.* **101**, 562–568 (2017).
197. Delgado-González, R., Astlas, A.S., Courtois, A. and Thollas, B. Exopolysaccharide for the treatment and/or care of the skin, mucous membranes and/or nails. US Patent 20160045423. Lipotec SA, Barcelona, and Polymaris Biotechnology, Brittany (2016).
198. Lipotec. *Hyanify™ marine ingredient* (2017). Available at: http://www.lipotec.com/en/products/hyanify-trade-marine-ingredient/, accessed 2 July 2017.
199. Lipotec. *Hyadisine® marine ingredient* (2017). Available at: http://www.lipotec.com/en/products/hyadisine-reg-marine-ingredient/, accessed 2 July 2017.
200. Rajput, N. Cosmetics market by category (skin & sun care products, hair care products, deodorants, makeup & color cosmetics, fragrances) and by distribution channel (general departmental store, supermarkets, drug stores, brand outlets) - global opportunity analysis and industry forecast, 2014-2022 (2016). Available at: https://www.alliedmarketresearch.com/cosmetics-market, accessed 5 July 2017.